STUDY OF EFFECTIVENESS, TOLERABILITY AND SAFETY OF INTRAVENOUS IRON SUCROSE IN IRON DEFICIENCY ANAEMIA IN POSTNATAL WOMEN

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT FOR

M.D DEGREE
BRANCH - II
OBSTETRICS & GYNAECOLOGY,
MADRAS MEDICAL COLLEGE,
CHENNAI - 3.

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI - 1.

MARCH 2010

CERTIFICATE

This is to certify that the dissertation titled "Study of effectiveness, tolerability and safety of intravenous iron sucrose in iron deficiency anaemia in postnatal women" submitted by Dr.R.Niranjana to the Faculty of Obstetrics and Gynaecology, Madras Meddical College, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (Obstetrics and Gynaecology) is a bonafide research work carried out by her under our direct supervision and guidance.

Dr.J.MOHANASUNDARAM,
M.D., Ph.D., DNB,
Dean,
Madras Medical College,
Chennai - 3.

Dr.REVATHY JANAKIRAM
M.D., DGO., MNAMS, FIMCH, FICOG
Director & Superintendent,
Institute of Obstetrics & Gynaecology,
Egmore, Chennai - 8.

DECLARATION

I. Dr. R.Niranjana, solemnly declare that the dissertation titled “Study of effectiveness, safety, tolerability of intravenous iron sucrose in iron deficiency anaemia in postnatal women” has been prepared by me.

This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in Obstetrics and Gynaecology. This has not been submitted previously by me for the award of any degree or diploma from any other university.

Dr. R.Niranjana.

Place: Chennai.
Date:

ACKNOWLEDGEMENT

I express my heartfelt gratitude to **Dr. Revathy Janakiram M.D, D.G.O., MNAMS**, professor and Director of the Institute of obstetrics and Gynaecology, Madras Medical College and Research Institute, Chennai for her great help, Inspiration and Encouragement, in conducting my study.

I am very Grateful to Prof. **Dr.Shanthi Dinakaran, MD., DGO,** Deputy Superintendant, Institute of Obstetrics and Gynaecology, for her guidance and encouragement.

My Profound thanks to **Dr. Mohana Sundaram, M.D., Ph.D., DNB,** Dean, Madras Medical College, Chennai for permitting me to utilise the clinical materials of the hospital.

My heartfelt thanks to **Dr. Kanchana, M.D., Pathologist,** Institute of obstetrics and Gynaecology for her support in conducting this study and to **Mr. P.Karunanithi kirupalani, M.Sc (Bio), M.Phil.,** Biochemist, Madras Medical College, Chennai.

I thank all my Assistant Professors for their help during this study.

The co-operation of the patients is gratefully acknowledged.

INDEX

INTRODUCTION

INTRODUCTION

Anaemia is defined by a decrease in haemoglobin concentration with a consequent decrease in the hematocrit. It is the most common medical disorder in pregnancy. The two most common cause of anaemia are iron deficiency and acute blood loss. (1)

Depending on the severity of the blood loss anaemic postpartum patients can be at increased risk of morbidity and even mortality (2) and anaemia due to heavy bleeding during delivery should be corrected without delay.

Anaemia is defined by World Health Organisation as haemoglobin levels <11 g/dl. It is one of the most serious global public health problems, affecting 52% of pregnant women in developing and 23% of the developed countries. (3)

Iron is an essential component of haemoglobin in the blood. The pregnant woman needs 1000mg of iron all through her pregnancy i.e. 3-5 mg/day to maintain iron balance. This demand during later half of pregnancy and for several weeks after delivery increases to 6.7 mg/day. (4)

The absorption of iron from oral supplements is influenced by the dose; the patients iron stores and intake in relation to meal time. Parentral administration of iron, as an alternative provides a quick and certain correction of total iron deficit. (5)

A complete workup is essential, preferably with haematological indices such as hypochromic and microcytic red cells and reticulocytes classified by degree of maturity in particular before parentral therapy is given. (6)

Traditional therapy which is based on either oral administration of iron or blood transfusion has had many draw backs. Efficacy of oral iron is limited due to high incidence of side effects and non-compliance where as blood transfusion is associated with the risk of infection, immunologic impact and transfusion reactions. (6)

Modern alternative strategies call for parentral administration of new, well tolerated iron preparation e.g., iron sucrose which has been successfully used in the treatment of postpartum anaemia and increasingly during 2^{nd} and 3^{rd} trimester of pregnancy. (6)

This study was done to find out the efficacy and safety of intravenous iron sucrose in the treatment of iron deficiency anaemia in the postpartum period.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

International journal of gynaec and obstetrics (2005) 90,238-239. A.Dede, D.Uygus, B.Yilmaz T.mungan, M.Ugur conducted a study to compare the safety and efficacy of intravenous iron sucrose complex in the treatment of iron deficiency anaemia during puerperium. The study population had 75 women older than 18 years whose haemoglobin were <= 9g/dl after delivery whether vaginal or caesarean. The participants were assigned to 2 groups. In the intravenous group, n=50 the total iron sucrose dose was administered as calculated. Those receiving oral treatment (n=25) were given 300 mg tablets of iron sulphate (each containing 60mg elemental iron) 1hour before meals three times a day. Blood samples were taken before the start of therapy and at days 7 and 28 to evaluate Hb%, serum ferritin, serum iron and CRP as well as hematocrit, mean corpuscular volume (MCV) and total serum iron binding capacity.

In conclusion, intravenous iron therapy with iron sucrose complex significantly increased serum ferritin level within a short time with fewer side effects than oral iron therapy in women with postpartum iron deficiency anaemia.

British journal of Obstetrics and Gynaecology, Sep 2006; 1248-1252. Bhandal.N.Russell. R carried out a prospective randomised trial enrolling 44 women with iron deficiency anaemia, defined as Hb < 9gm/dl when measured 24 to 48 hrs after delivery. Group A received (N.22) 200mg I.V on days 2 and 4. Group B (N. 22) received 200mg of oral ferrous sulphate twice a day for 6 wks. Average rise in Hb was 2.5gm/dl on day 5 in I.V group and 0.7gm/dl in oral group. There were no serious adverse effects in I.V group except a few who reported facial flushing and metallic taste during iron infusion. 1/3 of women in oral group had gastrointestinal side effects. They concluded that in women with postpartum iron deficiency anaemia intravenous iron sucrose produces higher blood Hb level than oral iron supplementation.

C Giannoulis, A Danniilides, T Tantanasis, K Dinas, and J Tzafettas. Intravenous administration of iron sucrose for treating anaemia in postpartum women. Hippokratia, 2009 Jan – Mar: 13(1): 38 – 40. The prsopective study was conducted in one hundred and four postpartum women. The criteria for the diagnosis of anaemia were Hb <8 g/dl and ferritin < 10µg/dl. They were randomised into two groups. Group A consisted of 78 women who received i.v a total amount of 300mg iron sucrose in three days. Group B

consisted of 26 women who received orally 800 mg iron protein succinylate daily for four weeks. At the end of study, in group A the increase in Hb mean level was 4.6 g/dl and of ferritin mean level was 105 mg/l. In group B the increase in Hb mean level was 2.3 g/dl and ferritin level was 68 mg/dl. The significant difference in the increase of haemoglobin level (p=0.0001) and also in the increase in ferritin level (p=0.0004) between the two groups.

Lippincott Williams and Wilkins Inc, Pakistan institute of medical science conducted a randomised controlled study in 80 patients with gestational age of 12 – 36 wks from antenatal clinic and 20 patients after postpartum haemorrhage with anaemia. Group A received I.V. iron sucrose; group B received I.M iron sorbitol. Group A had mean Hb content of 1.3 + 1.1 gm/dl and group B had 7.9 + 0.9 gm/dl. Three weeks post therapy assessment of Hb showed a total rise of 2.6 gm/dl (Group A) and 1.2 gm/dl (Group B). Target Hb i.e. 11gm/dl was achieved in 80% of group A and 20% of group B Patients. Blood transfusion was not required in any group. They concluded that intravenous iron sucrose is safe, convenient and more effective than intramuscular iron therapy in treatment of Iron deficiency anaemia during pregnancy. It can minimise blood transfusion in postnatal women.

scoff b. silverstein and george rodgers

The increased availability of parentral iron preparation should decrease the need to use red cell transfusion in patients with iron deficiency anaemia. They observed that increase in Hb is noted after one week of iron sucrose administration and serious anaphylactic hypersensitivity of 0.002% in i,v iron sucrose group compared to 0.6-0.7% in i,m iron dextran group.

Gravier A, Descargues G, Marpeace L et al (1999) conducted a study on how to avoid postpartum blood transfusions in Iron deficiency anaemia patients, by treating with I.V Iron sucrose. They concluded that I.V Iron sucrose is effective in preventing unnecessary blood transfusions in postpartum patients.

Al Momen et al conducted a prospective, open-label controlled trial in 111 pregnant women with iron deficiency anaemia (Hb : <9gm/dl) and divided into 2 groups. Intravenous group and intramuscular group. Intravenous iron sucrose was administered as an infusion of single 100mg dose in normal saline every 1 to 3 days.

Controls received I.M iron dextran (100mg on alternate days) till the calculated dose was reached. Intravenous iron therapy

resulted in higher levels of Hb, with the time to achieve maximum Hb in shorter period compared with controls. No serious adverse effects were noted in iron sucrose group whereas 6% of patients could not tolerate I.M iron dextran, who were excluded from the study. 30% of patients in the control group had disturbing G1 symptoms and 32% were non complaint.

Wali A, MushtaqA, Nilofer.(Journal Pakistan med. Assoc. 2002 sep 52(9): 392 – 5)

A prospective comparative study, total number of 60 pregnant women with gestational age of 12 – 34 wks with iron deficiency were included, and divided into 2 groups. Group A (N: 30) received intra venous iron sucrose according to recommended dose containing 500mg of iron sucrose for storage, Group B (n=30) received intramuscular iron dextran. Mean Hb in group A was 8.0+/- 1.1gm/dl and in group B was 8.8+/- 0.9gm/dl. In group A and B initial Hb was assessed 3 weeks after therapy which showed an average rise of 2.8gm/dl in group A and 1.4 gm/dl group B. Target Hb level of 11gm/dl was achieved in 80% of group A, 28% of group B patients. In group A one patient had moderate abdominal pain, 2 had weakness and shivering, 3 had phlebitis but none of the patients discontinued the therapy due to adverse effects.

In group B majority complained of pain at the injection site, in which 5 patients dropped out from study due to intolerance. They concluded that I.V iron therapy is safe, convenient and more effective than I.M iron therapy; hence I.V iron therapy can replace blood transfusion in antenatal period.

Breyman et al conducted a prospective randomised open study evaluated the efficacy and safety of intravenous iron sucrose with or without recombinant human erythropoietin in correcting iron deficiency anaemia (Hb <10gm/dl) in pregnant women ie. gestational age (> 21 weeks). 20 patients received recombinant human erythropoietin 300 IU/kg and iron sucrose 200mg I.V and 20 patients received I.V iron sucrose 200mg alone twice weekly for 4 weeks till a target Hb of 11 gm/dl was achieved. There was immediate reticulocyte response and progressive rise in hematocrit in both groups. Higher rise in reticulocyte count and rise in hematocrit was observed in the group that received combination therapy. None required blood transfusion. No serious adverse effects were reported. They concluded that intravenous iron sucrose alone should be considered first in resistant iron deficiency anaemia during pregnancy. Recombinant human erythropoietin may be

considered in severe anaemia requiring rapid correction, not responding to I.V iron sucrose.

Al-Momen Ak, al-Mechari A; al-Nuaime L et al in 1996 conducted an study comparing I.V iron sucrose and oral ferrous sulphate, they observed that iron sucrose complex group achieved significantly higher Hb level (128.5+/- 6.6gm/dl Vs 111.4 +/- 12.4g/l) in control group. P < or = 0.001. Iron sucrose complex showed no major side effects, but 6% of control group could not tolerate ferrous sulphate. 30% had poor compliance in the control group. They concluded that iron sucrose complex is safe and effective in the treatment of iron deficiency anaemia during pregnancy.

Catherine Gay (2005) concluded that although oral iron is the standard treatment for iron deficiency anaemia, it is poorly tolerated and has low efficacy in rapid correction of anaemia; But I.V iron sucrose is both quick and effective in treating anaemia. The average mean rise of Hb was 0.8 gm/dl for oral iron, 3.5 gm/dl for blood transfusion and 3.1gm/dl for I.V iron after 14 days. No serious adverse effects were noted for I.V iron sucrose.

Bayoumeu F, Subiran – Buisset E, Baka NE et al (2002) American Journal of obst. and Gynaecology also observed the effectiveness, safety and tolerability of I.V iron sucrose compared to oral iron for treatment of iron deficiency anaemia in pregnant women.

Chamate E. conducted a study on treatment of iron deficiency anaemia in pregnancy and immediate puerperium comparing I.V iron sucrose and oral ferrous sulphate and concluded that I.V iron sucrose is safe, convenient and more effective with less adverse effects and it can replace blood transfusion in antenatal period.

Al-Wakeel Js, Malik GH, Atmohaya S, et al 1997, also confirmed the effectiveness of intravenous iron sucrose in patients with iron deficiency anaemia.

Gabriela Bancaiova, Ursula Von Mandach, Roland Zimmerman- European journal of obstet and gynaecology and reproductive biology, vol 144 issue2 – June 2009; 135-139- done a study to compare the efficacy and safety of two or three doses of intravenous iron sucrose with daily oral ferrous sulphate in the prophylaxis of iron deficiency anaemia in pregnant women. 260 women with singleton pregnancy were randomised between the 21st

and 24 th week with either i,v or oral iron group. Of 130 women in the i,v group, 75 received 2 doses of 200mg iron sucrose, 55 three doses of 200mg iron sucrose. The first dose was administered between the 21st and 24th gestational week, the second between the 28th and 32nd and the third between 35th and 37th week. The women of oral group were given oral tablets of 80mg ferrous sulphate daily. They concluded that there was no clinically significant difference in the haematological maternal and foetal outcomes in the parentral route of iron prophylaxis in pregnant women.

IRON METABOLISM

The average daily intake of oral iron is 20mg and the amount of iron absorbed ranges normally from 3-6% of the amount ingested. (8).

SOURCES AND CONTENTS OF IRON

Milk/litre

- Human milk - 0.5mg
- Cow's milk - 0.02- 0.3 mg

Foods/100g

a. pulses 9-11mg
b. Cereals 4-11mg
c. Meat, fish 10-25mg
d. Ripe banana 0.9mg
e. Mango 1.3 mg
f. Melon 7.5mg (9)

ABSORPTION OF IRON

Iron is absorbed in the ferrous form (Fe2+) but most dietary iron is in the ferric form (Fe3+). Most of the iron is absorbed in the duodenum and the proximal jejunum. The mucosal cells have the

iron binding protein apoferritin which combines with iron and stored as ferritin. The iron which enters the plasma is bound to the iron transporting polypeptide transferrin. Apoferritin which is found in many other cells binds to form ferittin and stored. (8).

BIOAVAILABILITY OF IRON

Iron haemostasis is maintained in the short term by increased absorption of iron in deficiency situations and the amount of bioavailable iron present in the food is important in the long term. (10)

Food iron is present in most diets in a proportion of 6mg/1000 calories and is made of two different pools- heam and non-heam iron (10). The heam iron absorption is usually not affected by inhibitors.

The non-heam iron absorption is enhanced by heam, proteins, ascorbic acid and fermentation and decreased by inhibitors like phytic acid, fibres, calcium, tannins, tea, coffee, chocolate and herbal infusions.

Iron is important in human body because of its occurrence in many hematopoietins such as haemoglobin, myoglobin and cytochromes(9).

ERYTHROPOIESIS

The formation of red blood cells is subjected to feed back control. It is inhibited by a rise in the circulating red cell level to supernormal values and is stimulated by anaemia. It is also stimulated by hypoxia. (8).

Decrease in haemoglobin concentration due to various reasons causes decrease in arterial oxygen carrying capacity, which leads to increased erythropoietin production in kidney which stimulates erythropoiesis.

The reliability of in vitro bioassay is dependent on compensating for the modifying influences of other human serum components on erythropoietin activity when in vitro procedures are employed to measure erythropoietin in serum. (12).

Pleuripotent stem cell

↓

Committed stem cells
(Progenitor cell)

↓

GM – CSF erythroid series

↓

Pro erythroblast

↓

Rapid division

↓

Basophilic normoblast

↓

Polychromatic normoblast
(Proliferation activity ceases after this stage. It begins to produce Hb in the cell. They are called intermediate normoblast).

↓

Orthochromatic normoblast

(Final stage of maturation of nucleated red blood cells. Active Hb synthesis occurs in cytoplasm.

↓

Active extrusion of nucleus.

↓

Reticulocyte

↓

(Biconcave discoid shaped, greater volume and diameter than mature red blood cells)

↓

Lose their mitochondria and ribosome over the course of few days, lose the basophilic tint.

↓

Mature erythrocytes.

Transfusions of blood sufficient to raise the haemoglobin concentration above normal or prolonged inhalation of elevated partial pressure of oxygen results in depression of erythropoiesis in keeping with the expected consequences of such feedback system on regulation .(Finch et al 1970).

IRON DEFICIENCY ANAEMIA

Iron deficiency anaemia is the most common nutritional deficiency in pregnancy followed by folate deficiency anaemia. (13). Out of 150 million deliveries occurring annually in the world, approximately 6,00,000 women die from the complications of pregnancy. Anaemia is responsible for 40-60% of maternal deaths in non-industrialised countries. (14). Mothers with anaemia are more likely to succumb to the ill effects of haemorrhage, susceptible to infection and suffer from congestive cardiac failure. (15).

WHO criteria for diagnosis of anaemia in pregnancy is haemoglobin content of <11g/dl (7.45 mmol/l) and hematocrit of less than 0.33. CPC (centre for disease control, USA) proposes a cut off point of 10.5 g/dl during the second trimester (16).

ICMR CATEGORIES OF ANAEMIA

CATEGORY	SEVERITY Hb LEVEL (g/dl)
Mild	10.0 – 10.9
Moderate	7.0 – 10.0
Severe	< 7.0
Very severe	< 4.0

PREVALANCE OF ANAEMIA IN PREGNANCY

The overall prevalence of anaemia is estimated to 40% of the world's population. The prevalence is 35% for non pregnant woman and 51% for the pregnant woman globally and tends to be 3-4 times higher in non- industrialised than industrialised countries (17).

Nearly half of the global total number of anaemic woman live in the Indian sub continent and in India alone, the prevalence of anaemia during pregnancy may be as high as 88% (18).

IRON REQUIREMENT IN PREGNANCY

In an average pregnancy the requirements are

1. Basal iron – 280 mg
2. Expansion of red cell mass – 570 mg
3. Transfer to the fetus – 200 – 350 mg
4. Placenta – 50 -150 mg
5. Blood loss at delivery – 100-250 mg

After deducting the iron conserved by amenorrhoea (240 – 480 mg) an additional 500 to 600 mg iron is required in pregnancy or 4-6 mg per day of absorbed iron that is 2.5 mg per day in early pregnancy, 5.5 mg per day from weeks 20 – 32 and 6-8 mg per day from weeks 32 onwards (19).

CAUSES FOR HIGH PREVALANCE OF IRON DEFICIENCY ANAEMIA

1. Conception of low bioavailability diet. Iron deficiency was higher in both Hindu vegetarian and Muslim halal meat eaters, where the animal is slaughtered by cutting its carotid artery and bleed to death. (20)

2. Defective iron absorption due to worm infestation, amoebiasis and giardiasis is upto 40% and is a significant cause of abnormal iron metabolism and anaemia. (21)

3. Multiple pregnancies where the woman enters pregnancy with little or no iron reserve which is compounded by closely spaced pregnancies and prolonged lactation (22).

STAGES OF IRON DEFICIENCY ANAEMIA

Stage I: Negative iron balance

Demands for iron exceed the body's ability to absorb iron from diet.

Normal Hb / hematocrit level, Normal RBC indices

Serum Ferritin < 20ng/ml

Stage II: Iron deficient Erythropoiesis

When stores become depleted serum iron begins to fall, total iron binding capacity rises gradually and once the transferrin falls to 15 to 20%, Hb synthesis becomes impaired.

Stage III: Iron deficiency anaemia

Peripheral picture reveals microcytic and hypochromic cells appearing as vacuolated red blood cells with reticulocytes in circulation. Gradually Hb and hematocrit begins to fall. Transferrin saturation < 15%.

EFFECT OF ANAEMIA IN PREGNANCY

FETAL/PLACENTAL	MATERNAL
Prematurity	Reduced blood reserve
Premature uterine contractions	Low exercise and mental performance
Amnion rupture	Cardiovascular strain
Growth retardation	Tiredness
Abnormal trophoblast invasion	Reduced immune function, infection
Fetal programming	Negative thermo regulation
Disease in new born	Increased rate of blood transfusion(25)

Increased incidence of preterm labour (28.2%), pre-eclampsia (31.2%) and sepsis have been associated with anaemia (24). During labour there is an increased incidence of postpartum haemorrhage and congestive cardiac failure. During puerperium there is an increased chance of puerperal sepsis, subinvolution, failing lactation and venous thrombosis.

Fetuses tend to have decreased iron stores due to depletion of maternal stores. Adverse perinatal outcome in the form of preterm and small for gestational babies and increased perinatal mortality.(24)

CLINICAL FEATURES

1. Mild anaemia may not have any effect on pregnancy
2. Moderate anaemia may cause increased weakness, lack of energy, fatigue, and poor work performance
3. Severely anaemic woman may have palpitations, tachycardia, breathlessness, increased cardiac output leading on to cardiac stress which can cause decompensation and cardiac failure which may be fatal (15,20, 21, 23).

SIGNS

There may be no signs in mild anaemia. There may be pallor, glossitis and stomatitis. Patient may have oedema due to hypoprotinemia. Soft systolic murmur can be heard in the mitral area due to hyperdynamic circulation. There can be fine crepitation at the base of lungs due to congestion.

DIAGNOSIS

Haemoglobin estimation is the most practical method of diagnosis of anaemia. Though various methods like Taliquists method, copper sulphate method and sahli's method available, cyanmethhaemoglobin method appears to be the most accurate. (26).

Peripheral blood smear is another bedside indicator of diagnosis of anaemia which will also differentiate between iron deficiency anaemia, megaloblastic anaemia and haemolytic anaemia. Mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration are all low in the iron deficiency anaemia. (20). Although the assessment of iron status in human population is advanced compared with other nutrients, there is still a large uncertainty about absolute diagnosis during pregnancy. (27).

Parameters	Normal	-ve iron balance	Iron deficient erythropoiesis	Iron deficiency anaemia
Marrow iron status	1 -3+	0 – 1+	0	0
Serum ferritin (ng/ml)	50 – 200	<20	<15	<15
TIBC(mg/dl)	300 –360	>360	>380	>400
Serum iron(mg/dl)	50 – 150	N	<50	<30
Saturation (%)	30 – 50	N	<20	<10
Marrow sideroblast(%)	40 – 60	N	<10	<10
RBC protoporphyrin (mg/dl)	30 – 50	N	>100	>200
RBC morphology	N	N	N	Microcytic hypochromic

ORAL IRON PROHYLAXIS IN PREGNANCY

The policy of oral iron prophylaxis varies in different countries.

The WHO recommendation is based on the prevalence of anaemia. 60 mg of elemental iron with 400 microgram of folic acid per day is recommended for 6 months where the prevalence of anaemia in pregnancy is <40% and this dose to be supplemented for another 3 months postpartum in areas where the prevalence is >40%. (19)

The National Nutritional Anaemia Control Programme of India recommends 100 mg of elemental iron plus 500 microgram of folic acid for prophylactic supplementation for a minimum of 100 days starting in the second trimester and double this dosage for the treatment of anaemia i.e. 200 mg of elemental iron and 1000 microgram of folic acid. (28).

TREATMENT

The most common cause of anaemia in pregnancy is due to iron deficiency. Iron treatment can be given by mouth, or an injection into the muscle (intramuscular) or into the vein (intravenous). (29).

Traditional therapy which is based on either oral administration of iron or blood transfusion or both has had drawbacks. The efficacy of orally administered high dose iron was limited by the high incidence of side effects and thus non compliance whereas blood transfusion remains a last resort because of patient choice and the risk of infection, immunologic impact and transfusion reaction. (6)

Recently there is increasing interest on alternative therapeutic option which includes use of parentral iron sucrose complex and recombinant human erythropoietin. (30, 31, 32, 33).

Parentral iron sucrose complex has several advantages because it has a low allergenic properties with a extremely low incidence of severe side effects such as anaphylactic reactions (34,35)

Iron sucrose complex has a high availability for erythropoeisis, little renal excretion (<5%) and low tissue accumulation and toxicity. (36).

PHARMACOLOGY OF IRON SUCROSE

IRON SUCROSE

Chemical Formula

$[Na_2\ Fe_5O_8\ (OH)\ 3\ (H2o)]_n\ .\ m(C_{12}\ H_{22}\ O_{11})$

Iron sucrose is a brown, sterile, aqueous complex of polynuclear iron (III) hydroxide in sucrose containing 20mg elemental iron per ml.

The sterile solution has an osmolarity of 1250 mosm/l. The product does not contain preservatives.

Molecular wt: 34,000 – 60,000 daltons

pH : 10.5 – 11.1

MECHANISM OF ACTION

Following intravenous administration, it is dissociated into iron and sucrose by reticuloendothelial system and iron is transferred from the blood into pool of iron in the liver and bone marrow. Ferritin sequesters iron in a nonionic form from which iron is easily available.

PHARMACOKINETICS

Its iron component exhibits first order kinetics

Elimination t ½	: 6 hrs
Total clearance	: 1.2 litres / hour
Non – steady state apparent volume of distribution	: 10 lit
Steady state apparent volume of distribution	: 7.9 lit.

DISTRIBUTION

In healthy adults, its iron component appears to distribute mainly in blood and to some extent in extra cellular fluid.

ELIMINATION

The sucrose component is eliminated mainly by urinary excretion. Some iron is also eliminated in the urine. (approximately 5%)

SIDE EFFECTS

Headache, fever, pain, asthenia, malaise, abdominal pain.

INTERACTION

Should not be administered concomitantly with oral iron preparation since the absorption of oral iron may be reduced.

CONTRAINDICATIONS

1. Evidence of iron over load.

2. Anaemia not caused by iron deficiency

3. Known hypersensitivity to I.V iron sucrose (or) any of its inactive compounds.

METHOD AND ROUTE OF ADMINISTRATION

No test dose is required

1. Slow IV injection

100mg (2amp) to be given undiluted over a period of 2 – 5 min.

2. Slow IV infusion

100mg (2amp) to be diluted with 100ml of normal saline immediately prior to infusion and to be infused over a period of atleast 15min (6mg/min).

DOSAGE FREQUENCY

100mg/day given on alternate days until the required dose is infused.

Chandler et al observed that optimal doses of 200 – 300mg infused intravenously over 2 hrs were well tolerated and safe.

Patients who received a dose of 400 – 500mg intravenously over 2 hrs experienced hypotension, nausea, and low back pain.

SUPPLY AND STORAGE

Supplied as 2.5ml single dose vial. Each 2.5ml vial contains 50mg of elemental iron (20mg/ml) that is packaged in carton containing 10 single dose vials. Stored at 25^0C. Excursions permitted to 15 – 30^0C.

AIM OF THE STUDY

1. To determine the efficacy and tolerability of the intravenous iron sucrose in the treatment of iron deficiency anaemia in the postpartum period.

2. To determine the safety of iron sucrose in the treatment of iron deficiency anaemia in the postpartum period.

MATERIALS AND METHODS

This study was conducted in Institute of Obstetrics and Gynaecology, Madras Medical College, Chennai. Fifty (50) postnatal patients both after vaginal and caesarean section with iron deficiency anaemia within the first 48 hours with haemoglobin percentage between 6 g/dl and 8g/dl were selected and included in this study.

INCLUSION CRITERIA

1. Age > 18 years
2. Diagnosis of postpartum anaemia with Hb% equal to or greater than 6 g/dl and less than 8 g/dl.

EXCLUSION CRITERIA:

1. History of allergy to iron containing medications
2. History of allergic conditions or bronchial asthma
3. Thalassemia
4. History of bleeding tendency
5. Non iron deficient anaemia

Blood investigations were sent for the patients who looked clinically anaemic within the first 48 hours of either vaginal or

caesarean delivery, which includes Hb%, PCV, MCV and tests to confirm iron deficiency anaemia by peripheral smear, serum iron and total iron binding capacity.

Hb%, PCV, MCV were analysed by automatic cell counter and serum iron and total iron binding capacity were calculated using semi auto analyser ERBA CHEM 5 PLUS V2.

Those patients with iron deficiency anaemia were included in this study. An informed consent was obtained, a detailed history taking and a complete general examination was done.

METHOD OF THE STUDY

The dosage of iron required for each individual patient is calculated using the formula

(Target Hb% - patient Hb %) in gm% * 2.4 *weight in kg

Test dose is not needed. The patients were given 100 mg of elemental iron diluted in 100 ml of 0.9 % normal saline and infused over 15 minutes every alternate day (not more than 3 days in a week) until the required dosage is infused.

OBSERVATION

During therapy the following parameters were monitored.

1. Vitals – temperature, pulse rate, blood pressure
2. Adverse effects like nausea, vomiting, abdominal pain, chills, etc
3. Anaphylactic reactions

The following investigations were done before starting therapy,

1. Haemoglobin in g/dl
2. PCV
3. MCV
4. Serum Iron
5. Total iron binding capacity
6. Peripheral smear

Patients were discharged after infusing the required dose of iron and asked to attend the postnatal clinic after four weeks of therapy and the following parameters were assessed.

1. Haemoglobin in g/dl
2. Hematocrit
3. MCV
4. Serum iron
5. TIBC.

RESULTS

Fifty postnatal women after confirming iron deficiency anaemia were included in this study and the required dosage of iron was infused intravenously in the form of iron sucrose complex.

CHARACTERISTICS OF THE CASES STUDIED:

Table: 1: AGE DISTRIBUTION

AGE	N	PERCENTAGE
<= 20	4	8%
21 – 25	26	52%
26 – 30	16	32%
>30	4	8%
TOTAL	50	100%

Among the fifty(50) women studied, 8% (4/50) were less than or equal to 20 years , 52% (26/50) of the patients belong to the age group between 21 - 25 years, 32% (16/50) of the patients belong to the age group between 26 – 30 years and 8% (4/50) belong to age group above 30 years. The mean age group in our study was 24.94 years.

Table: 2: SOCIO ECONOMIC STATUS

SOCIO ECONOMIC CLASS	N	PERCENTAGE
CLASS I	-	-
CLASS II	-	-
CLASS III	-	-
CLASS IV	8	16%
CLASS V	42	84%
TOTAL	50	100

Among the fifty patients in our study 84% (42/50) belonged to the class V socio economic status who were more prone for nutritional deprivation and 16% (8/50) belonged to the class IV socio economic status and none belonged to the class I, II and class III.

Table- 3: BOOKING STATUS:

BOOKING STATUS	N	PERCENTAGE
BOOKED	36	72%
UNBOOKED	14	28%
	50	100%

Among the fifty patients included in our study 72% (36/50) were booked and 28% (14/50) were unbooked.

Table - 4: PARITY

PARITY	N	PERCENTAGE
PARA I	16	32%
PARA II	28	56%
PARA III	06	12%
	50	100%

Among the fifty postnatal patients included in our study 32% (16/50) were primipara and 68% (34/50) were multipara. Among them 56% (28/50) were para two and 12% (6/50) were para three.

Table - 5: MODE OF DELIVERY

S.NO	MODE OF DELIVERY	NO	PERCENTAGE
1	Labour natural	11	22%
2	Labour natural with episiotomy	16	32%
3	Labour natural with LP	1	2%
4	Emergency LSCS	10	20%
5	Emergency repeat LSCS	3	6%
6	Emergency repeat LSCS with St.	9	18%
		50	100%

Among the fifty postnatal patients in our study 56% (28/50) delivered vaginally and 44% (22/50) were delivered by caesarean section. Among the vaginal deliveries 22% (11/50) delivered as labour natural with intact perineum, 32% (16/50) delivered by labour natural with episiotomy, and 2%(1/50) delivered by labour natural with lacerated perineum. Among the caesarean sections 20% (10/50) were emergency caesareans, 6%(3/50) were emergency repeat caesareans and 18%(9/50) were emergency repeat caesarean sections with sterilisation.

Table - 6: CHANGE IN HAEMOGLOBIN %

	N	**MEAN Hb%**	**STD. DEVIATION**
Before treatment	50	7.3020	0.63455
After treatment	50	10.9040	0.90935
Change in Hb%		3.6020	0.63551
p Value	p = 0.000 significant		

Mean haemoglobin among the fifty patients before starting the therapy was 7.3020 g/dl and the mean haemoglobin % at the end of one month of completing the therapy was 10.9040 g/dl. The rise in mean haemoglobin i.e. the difference in the mean haemoglobin before and after treatment was 3.6020 g/dl. The p value is 0.000 which is statistically significant.

Table - 7: CHANGE IN HEMATOCRIT

	N	MEAN PCV	STD.DEVIATION
Before treatment	50	24.3520	3.06802
After treatment	50	33.0900	2.17549
Change in mean PCV		8.7380	2.66817
p Value	p=0.000 significant		

The mean hematocrit of the fifty patients studied before starting the treatment was 24.3520 with a standard deviation of 3.06802. The mean hematocrit after completing the therapy was 33.0900 with a standard deviation of 2.17549. The difference in the mean hematocrit was 8.7380 with a p value of 0.000 which is statistically significant

Table - 8: CHANGE IN MCV

	N	MEAN MCV	STD.DEVIATION
Before treatment	50	73.2660	5.63269
After treatment	50	86.8200	3.12782
Change in mean MCV		13.5540	5.40110
p Value	P= 0.000 Significant		

The mean MCV (Mean Corpuscular Volume) of the fifty patients before starting the treatment was 73.2660 with a standard deviation of 5.63269. The mean MCV after the completion of the treatment was 86.8200 with a standard deviation of 3.12782. The difference in the mean MCVs was 13.5540 with the p value of 0.000 ($p<0.05$) which is statistically significant.

Table - 9: CHANGE IN SERUM IRON

	N	MEAN SERUM IRON	STD DEVIATION
Before treatment	50	57.9560	5.11744
After treatment	50	96.7720	7.56180
Change in mean		38.8160	7.32606
p Value	p=0.000 Significant		

The mean serum iron of the fifty patients before starting the treatment was 57.9560 with a standard deviation of 5.11744. The mean serum iron after completion of the therapy was 96.7720 with a standard deviation of 7.56180. The difference in the mean serum iron values was 38.8160 and p value was 0.000 ($p<0.05$) which was statistically significant.

Table - 10: CHANGE IN TIBC

	N	MEAN TIBC	STD.DEVIATION
Before treatment	50	399.0300	21.90894
After treatment	50	269.2600	36.98417
Change in mean		129.7700	38.87024
p Value	p= 0.000 significant		

The mean total iron binding capacity of the fifty patients before starting the treatment was 399.0300 with a standard deviation of 21.90894. The mean total iron binding capacity after the completion of the therapy was 269.2600 with a standard deviation of 36.98417. The difference in the mean total iron binding capacity before and after treatment was 129.7700 and the p value was 0.000 ($p<0.05$) which was statistically significant.

Table - 11: CHANGE IN PERCENT SATURATION

	N	MEAN % SATURATION	STD.DEVIATION
Before treatment	50	14.4780	1.63860
After treatment	50	36.7406	6.62209
Change in mean		22.2626	6.12970
p Value	p= 0.000 Significant		

The mean percent saturation of the fifty patients before starting the treatment was 14.4780% with a standard deviation of 1.63860. The mean percent saturation after the completion of the therapy was 36.7406 with a standard deviation of 6.62209. The difference in the two means was 22.2626 and the p value was 0.000 ($p<0.05$) which was statistically significant.

TABLE - 12: ADVERSE EFFECTS OF THE DRUG

S.NO	ADVERSE REACTIONS	N	PERCENTAGE
1	Head ache	1	2%
2	Nausea/vomiting	-	-
3	Abdominal pain	-	-
4	Chills and rigors	3	6%
5	Joint pain	-	-
6	Thrombophlebitis	2	4%
7	Pain at injection site	-	-
8	Anaphylactic reactions	-	-
9	No side effects	44	88%

Among the fifty (n=50) postnatal patients in this study, the side effects were very minimal and seen in only 12% (6/50). They were headache in 2% (1/50) patients, chills and rigors in 6% (3/50) and thrombophelibitis in 4% (2/50) patients. There were no anaphylactic reactions noted in the study group. There were no adverse effects noted in 88% (44/50) of the patients.

DISCUSSION

In our study fifty postnatal patients with iron deficiency anaemia were selected according to the inclusion and the exclusion criteria stated in the methodology. The iron required is calculated and given intravenously in the form of iron sucrose complex and followed up after 30 days and the results are analysed.

In our study 8% (4/50) of the patients were less than or equal to 20 years , 52% (26/50) of the patients belong to the age group between 21 - 25 years, 32% (16/50) of the patients belong to the age group between 26 – 30 years and 8% (4/50) belong to age group above 30 years. The mean age group in our study was 24.94 years.

In our study 84% (42/50) belonged to the class v socio economic status who are more prone for nutritional deprivation and 16% (8/50) belonged to the class Iv socio economic status and none belonged to the class I, II and class III. Hence all were in the low socio economic status.

In our study 72% (36/50) were booked and 28% (14/50) were unbooked.

In our study 32% (16/50) were primipara ,56% (28/50) were para two and 12% (6/50) were para three. Majority were in the multiparous group 68% (34/50).

COMPARISION OF OUTCOME PARAMETERS

Change in Haemoglobin %

In our study which included fifty postnatal patients the mean haemoglobin before starting treatment was 7.3020 and after four weeks of treatment was 10.9040 with a p value of 0.000 ($p<0.05$) which was statistically significant. The average raise in the Hb% in the four weeks time was 3.6020 with a p value <0.05 which was statistically significant.

According to a study by N Bhandal R Russel et al at Department of Anaesthesia, Nuffield department of anaesthetics, John padcliffe hospital, Oxford, UK, a prospective randomised control trial which included forty four (44) postnatal women with Hb<9g/dl at 24 – 48 hours post delivery. The mean Hb% before starting the therapy was 7.5g/dl and at the 40^{th} day post treatment was 11.2 g/dl with a p value of <0.01 which was statistically significant. Our study was comparable to this study.

According to another study by C Giannoulis, A Danniilides, T Tantanosis et al art Department of Obstetrics and Gynaecology , Aristotle University of Thessaloniki, Greece – which included one hundred and four anaemic postpartum women with Hb < 8g/dl and ferritin <10 microgram /dl. The study compared the effect of intravenous iron sucrose over oral iron therapy at the end of four weeks. The increase in the mean Hb% was 4.6g/dl and mean ferritin level was 105mg/dl with a p value of 0.0001 which was statistically significant. Our study was comparable to this study.

Our study could be compared to a study by A.Dede, D.Uygut et al at the Zakai Tahi Burak Women's Health Education and Research Hospital, Division of Perinatology, Turkey, which included seventy five (n=75) postnatal women with Hb <9g/dl after delivery whether vaginal or caesarean and compared the effect of intravenous iron sucrose complex versus oral ferrous sulphate and compared the results at the end of 28 days. The mean Hb% at the start of treatment was 8.2+/- 0.6g/dl in both the groups. But the mean raise in Hb% at the end of 28 days was 12.5+/-1.6g/dl and 11.8+/-0.7 g/dl in the intravenous and oral group respectively. P value was 0.200 which was not significant. However the raise in mean Hb in the intravenous group was 4.3g/dl.

CHANGE IN HEMATOCRIT

The mean hematocrit of the fifty patients studied before starting the treatment was 24.3520 with a standard deviation of 3.06802. The mean hematocrit after completing the therapy was 33.0900 with a standard deviation of 2.17549. The difference in the mean hematocrit was 8.7380 with a p value of 0.000 ($P<0.05$) which is statistically significant

CHANGE IN MCV

In our study the mean MCV (Mean Corpuscular Volume) of the fifty patients before starting the treatment was 73.2660 with a standard deviation of 5.63269. The mean MCV after the completion of the treatment was 86.8200 with a standard deviation of 3.12782. The difference in the mean MCVs was 13.5540 with the p value of 0.000 ($p<0.05$) which is statistically significant.

Our study could be compared to a study by A.Dede, D.Uygut et al at the Zakai Tahi Burak Women's Health Education and Research Hospital, Division of Perinatology, Turkey, which included seventy five (n=75) postnatal women with Hb <9g/dl after delivery whether vaginal or caesarean and compared the effect of intravenous iron sucrose complex versus oral ferrous sulphate and compared the results at the end of 28 days. The mean MCV before

starting the treatment was 51.6+/- 7.2 and the mean MCV at 28 days post treatment was 84.9+/-2.2 and the mean raise was 33.3 which is significant.

In another study by Mrs. Khurshid shabir Raja et al, Jouranl of Pakisthan Med.Assoc. volume 28. Number 2 July – Dec 2003, which included fifty pregnant women with iron deficiency anaemia (Hb < 8g/dl), the mean MCV before starting the treatment was 65fl and mean MCV after the treatment was 75fl. The raise in mean MCV was 10fl with a p value <0.05 which is statistically significant. This is comparable to our study.

CHANGE IN SERUM IRON

In our study the mean serum iron of the fifty patients before starting the treatment was 57.9560 with a standard deviation of 5.11744. The mean serum iron after completion of the therapy was 96.7720 with a standard deviation of 7.56180. The difference in the mean serum iron values was 38.8160 and p value was 0.000 ($p<0.05$) which was statistically significant.

Our study could be compared to a study by A.Dede, D.Uygut et al at the Zakai Tahi Burak Women's Health Education and Research Hospital, Division of Perinatology, Turkey, which

included seventy five (n=75) postnatal women with Hb <9g/dl after delivery whether vaginal or caesarean and compared the effect of intravenous iron sucrose complex versus oral ferrous sulphate and compared the results at the end of 28 days. The mean serum iron values before starting the treatment was 42.8+/-29.3 and the mean serum iron 28 days post treatment was 86.2+/-44.3.

CHANGE IN TIBC

The mean total iron binding capacity of the fifty patients before starting the treatment was 399.0300 with a standard deviation of 21.90894. The mean total iron binding capacity after the completion of the therapy was 269.2600 with a standard deviation of 36.98417. The difference in the mean total iron binding capacity before and after treatment was 129.7700 and the p value was 0.000 ($p<0.05$) which was statistically significant.

Our study could be compared to a study by A.Dede, D.Uygut et al at the Zakai Tahi Burak Women's Health Education and Research Hospital, Division of Perinatology, Turkey, which included seventy five (n=75) postnatal women with Hb <9g/dl.The total serum iron binding capacity before starting the treatment was 411.0+/-105.2 and the mean TIBC after 28 days of treatment was 287.2+/-89.1.

CHANGE IN PERCENT SATURATION

In our study the mean percent saturation of the fifty patients before starting the treatment was 14.4780% with a standard deviation of 1.63860. The mean percent saturation after the completion of the therapy was 36.7406 with a standard deviation of 6.62209. The difference in the two means was 22.2626 and the p value was 0.000 ($p<0.05$) which was statistically significant.

ADVERSE REACTIONS

In our study which included fifty (n=50) postnatal patients in this study, the side effects were very minimal and see in only 12% (6/50). They were head ache in 2% (1/50) patients, chills and rigors in 6% (3/50) and thrombophelibitis in 4 (2/50) patients. There were no anaphylactic reactions noted in the study group. There were no adverse effects noted in 88% (44/50) of the patients.

In a study by N Bhandal,R Russel et al , no serious adverse effects were reported. Five women (23%) complained of metallic taste during the infusion of the drug which is not noted in our study. Four women (18%) complained of facial flushing, describing it as warm tingling sensation, this was reported as ‘not unpleasant’. There was no hemodynamic disturbance observed either during infusion or after infusion.

In a study by C Giannoulis, A Danniilides, T Tantanosis et al at Department of Obstetrics and Gynaecology, Aristotle University of Thessaloniki, Greece, reported that iron sucrose is quite safe for the liver in daily doses of 100mg, in comparison with other iron supplementation. Rare anaphylactic reactions because of the use of iron sucrose have been reported in about 0.002% of cases.

In another study by Dr. Mrs. Khurshid shabir Raja et al, published in Journal of Pakistan Med. Assoc. volume 28. Number 2 July – Dec 2003, which included fifty pregnant women with iron deficiency anaemia (Hb < 8 g/dl), only two patients, had mild reactions. One had pain in the epigastrium and the other had restlessness. No patient had reactions of severe nature, threatening the patient's life and requiring discontinuation of infusion.

SUMMARY

In our study fifty postnatal patients with iron deficiency anaemia were selected according to the inclusion and the exclusion criteria stated in the methodology. The iron required is calculated and given intravenously in the form of iron sucrose complex and followed up after 30 days and the following parameters were analysed.

1. Haemoglobin in g/dl.
2. Hematocrit.
3. Mean corpuscular volume.
4. Serum iron.
5. Total iron binding capacity.
6. Percent saturation.

The results of the study are tabulated, analysed and summarised as follows;

1. Majority of the patients around 52% (26/50) belong to the age group between 21 – 25 years.

2. Almost three fourth (72%) of the patients were booked patients.

3. Majority of the patients (84%) belongs to the class V socio economic status.

4. Majority of the patients were multipara (68%) and among them para 2 is the major population (56%)

5. Mean raise in haemoglobin % after 30 days of treatment was 3.60 with a p value <0.05 which is statistically significant.

6. Average raise in the mean hematocrit was 8.73 after 30 days of treatment with a p value <0.05 which is statistically significant.

7. Mean raise in the Mean Corpuscular Haemoglobin was 13.55 fl with a p value of <0.05 which is statistically significant.

8. Mean raise in the serum iron value was 38.82 with a p value <0.05 which is statistically significant.

9. Mean change in the total iron binding capacity is 129.77 with a p value of <0.05 which is statistically significant

10. Mean change in the percent saturation was 22.26 with a p value <0.05 which is statistically significant.

11. The side effects were very minimal in our study group (12%). The side effects profile was also very mild which included headache in one patient, chills and rigors in three patients and thrombophlebitis in two patients. No anaphylactic reactions occurred.

CONCLUSION

1. Intravenous iron sucrose complex is highly efficacious in improving the haemoglobin %, hematocrit and the serum iron values in the treatment of iron deficiency anaemia in the postnatal women.

2. Iron sucrose infusion was well tolerated and safe, there were no major adverse reactions

To conclude intravenous iron sucrose complex is safe, convenient and more effective mode of treatment of iron deficiency anaemia in postnatal women.

It could be used to reduce the number of blood transfusions in the postnatal period in asymptomatic women with Hb% between 6 and 8 g/dl.

BIBILIOGRAPHY

1. Bashiri A, Burstein E, Sheiner E, Mazor M. Anaemia during pregnancy and treatment with intravenous iron; Review of literature, Eur J Obstet gynaecol Reprod Biol 2003; 110; 2-7.

2. Breymann C, Zimmerman R, Hutch R, Hutch A. Use of recombinant human erythropoietin in combination with parentral iron in the treatment of postpartum anaemia. Eur J Clin Invest. 1996; 26: 123-30

3. World Health Organisation. Report of a WHO group of experts on nutritional anaemia. Technical report series no.503: WHO.1972.

4. Turmen T, AbouZahr C. Safe motherhood. Int J Gynaecol Obstet 1994; 46: 145-153.

5. Hallak M, Sharon AS,Diukman R, Aislender R, AbraMovici H. Supplementing iron intravenously in pregnancy; a way to avoid blood transfusion, J Reprod Med 1997; 42: 99-103.

6. Christian Breymann MD, Treatment of iron deficiency anaemia in pregnancy and postpartum with special focus on

intravenous iron sucrose complex. J Med Assoc Thai 2005; 88 (suppl 2): s108-9

7. Cochrane Database Syst Rev, 2006; 3: CD004736.

8. William F. Ganaong, Review of Medical Physiology 18th edition, Digestion and absorption; 447.

9. Harpers illustrated biochemistry ; 26th edition.

10. Hulten LE, Gramatkovski A, Gleerup A, Hallberg L. Iron absorption from the whole diet. Relation to meal composition, iron requirement and iron stores. Eur J Clin Nutr 1995; 49: 794-808.

11. Hallberg L, Bjorn Rassmussen E. Determination of iron absorption from whole diet. A new tool model using two radiation isotopes given as heam and non-heam iron. Scand J Haemato 1972; 9: 193-197.

12. Dekerk et al 1978, Fiskin and Russsel 1983.

13. Diejomaeoh FME, Abdulaziz A, Adekile AD. Anaemia in pregnancy. Int J Gynaecol Obstet 1994; 65: 299-301.

14. World Health Organisation. Revised 1990. Estimate of maternal mortality. WHO/ FRH/ MSM/ 96.1. Geneva: WHO:1996.

15. Bhatt R. Maternal mortality in India- FOGSI-WHO study. J Obstet Gynaecol Ind 1997; 47: 207-214.

16. Viteri FE. The consequences of iron deficiency and anaemia in pregnancy. Adv Exp Med Biol 1994; 352: 127-139.

17. World Health Organisation. The prevalence of anaemia in women. A tabulation of available information. Geneva; WHO: 1992.

18. Abel R, Rajarathinam J, Sampath kumar V. Anaemia in pregnancy. Impact of iron, deworming and DEC, RUSHA dept. Tamilnadu: CMC vellore 1999.

19. Stoltzfus R, Dreyfuss ML. Guidelines for the use of iron supplements to prevent and treat iron deficiency anaemia. Geneva: INACG, WHO, UNICEF 1998.

20. Sharma JB. Medical complications in pregnancy, In: sharma JB (ed). The Obstetric protocol, 1st edn. Delhi: Jaypee Brothers, 1998; 78-98.

21. Sharma JB, Arora BS, Kumar S, Goel S, Dhanuja A. Helminth and protozoan intestinal infection: an important cause of anaemia in pregnancy- women in Delhi. J Obstet Gynaecol Ind 2001; 51(6): 58-61.

22. Prema k, Neela KS, Ramalakshmi BA. Anaemia and adverse obstetric outcome. Nutr Rep Int 1981; 23: 637-643.

23. Indian Council of Medical Research. Evaluation of the National Nutritional Anaemia Prophylaxis Programme. Task force study. New Delhi: ICMR 1989.

24. Lops VR, Hunter LP, Dixon LR. Anaemia in pregnancy. Am Fam Physician 1995; 5: 1189-1197.

25. Christian Breymann. Iron deficiency and anaemia in pregnancy: Modern aspects of diagnosis and therapy. Blood cells, molecules and diseases (2002) 29(3) nov/dec 506-516.

26. Bhatt RV. Anaemia in pregnancy, early diagnosis and treatmen. J Int Med Assoc .1995; 93: 80-82.

27. American journal of clinical nutr.1994: 59 (suppl) 5025-103.

28. Indian Council of Medical Research. Supplementation trial in pregnant women with 60mg, 120mg, and 180mg iron with

500 microgram of folic acid. Indian Council of Medical Research, New Delhi, 1992, p.641.

29. Reveiz L, Gyte GML, Cuervo LG. Treatment of iron deficiency anaemia in pregnancy. Cochrane Database of systemaic review 2007, issue 1 Art no: CD003094. Do1: 10-1002/ 14651858.CD003094.pub .2.

30. Breymann C (2002). Iron supplementation during pregnancy. Fetal and maternal medicine reviews 13(1) 1-29.

31. Breymann C, Major A, Richter C, Hutch R, and Hutch A (1995). Recombinant human erythropoietin and parentral iron in the treatment of pregnancy anaemia, a pilot study. J Perinat Med. 23, 89-98.

32. Vora M., and Gruslin A, (1998) Erythropoeitin in Obstetrics. Obstetrical and Gynaecological survey 53 (8), p. 500-508.

33. Al Momen AK, al-Meshari A., al-Nuaim L., Saddique ,A., Abotalib Z, Khashogji T, and Abbas M, (1996). Intravenous iron sucrose complex in the treatment of iron deficiency anaemia during pregnancy. Eur J Obstet Gynaecol Reprod Biol 69, 121-124.

34. Danielson , B.G, Salmonson ,T., Derendorf, H., and Geisser, p. (1996). Pharmacokinetics of iron(III) hydroxide sucrose complex after a single intravenous dose in healthy volunteers. Arzneimitterforschung 46 (6), 615-621.

35. N Bhandal, R Russel et al. Intravenous versus oral iron therapy for postpartum anaemia. British journal of Obstetrics and Gynaecology, sep 2006; 1248-1252.

36. Dede, D. Uygur, B. Yilmaz, T. Mungan, M.Ugur. Intravenous iron sucrose complex versus oral ferrous sulphate for postpartum iron deficiency anaemia. International Journal of Gynaecology and Obstetrics (2005) 90,238 -239.

37. C Giannoulis, A Danniilides, T Tantanasis, K Dinas, and J Tzafettas. Intravenous administration of iron sucrose for treating anaemia in postpartum women. Hippokratia, 2009 Jan – Mar: 13(1): 38 – 40.

38. Dr. Mrs. Khurshid shabir Raja et al, Intravenous iron sucrose complex therapy in iron deficiency anaemia in the pregnant women. Journal of Pakistan Med. Assoc. volume 28. Number 2 July – Dec 2003.

ABBREVATIONS

WHO	-	World Health Organisation
Hb	-	Haemoglobin
MCV	-	Mean Corpuscular Volume
PCV	-	Packed Cell Volume
RBC	-	Red Blood Corpuscles
MCHC	-	Mean Corpuscular Haemoglobin Concentration
TIBC	-	Total Iron Binding Capacity
Fe2+	-	Ferrous Iron
Fe3+	-	Ferric Iron
I.V	-	Intravenous
LP	-	Lacerated Perineum
LSCS	-	Lower Segment Caesarean Section

ACKNOWLEDGEMENT

I express my heartfelt gratitude to **Dr. Revathy Janakiram M.D, D.G.O., MNAMS**, professor and Director of the Institute of obstetrics and Gynaecology, Madras Medical College and Research Institute, Chennai for her great help, Inspiration and Encouragement, in conducting my study.

I am very Grateful to Prof. **Dr.Shanthi Dinakaran, MD., DGO,** Deputy Superintendant, Institute of Obstetrics and Gynaecology, for her guidance and encouragement.

My Profound thanks to **Dr. Mohana Sundaram, M.D., Ph.D., DNB,** Dean, Madras Medical College, Chennai for permitting me to utilise the clinical materials of the hospital.

My heartfelt thanks to **Dr. Kanchana, M.D., Pathologist,** Institute of obstetrics and Gynaecology for her support in conducting this study and to **Mr. P.Karunanithi kirupalani, M.Sc (Bio), M.Phil.,** Biochemist, Madras Medical College, Chennai.

I thank all my Assistant Professors for their help during this study.

The co-operation of the patients is gratefully acknowledged.

CERTIFICATE

This is to certify that the dissertation titled “Study of effectiveness, tolerability and safety of intravenous iron sucrose in iron deficiency anaemia in postnatal women” submitted by Dr.R.Niranjana to the Faculty of Obstetrics and Gynaecology, Madras Meddical College, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree (Obstetrics and Gynaecology) is a bonafide research work carried out by her under our direct supervision and guidance.

Dr.J.MOHANASUNDARAM,
M.D., Ph.D., DNB,
Dean,
Madras Medical College,
Chennai - 3.

Dr.REVATHY JANAKIRAM
M.D., DGO., MNAMS, FIMCH, FICOG
Director & Superintendent,
Institute of Obstetrics & Gynaecology,
Egmore, Chennai - 8.

DECLARATION

I. Dr. R.Niranjana, solemnly declare that the dissertation titled “Study of effectiveness, safety, tolerability of intravenous iron sucrose in iron deficiency anaemia in postnatal women” has been prepared by me.

This is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in Obstetrics and Gynaecology. This has not been submitted previously by me for the award of any degree or diploma from any other university.

Dr. R.Niranjana.

Place: Chennai.
Date:

STUDY OF EFFECTIVENESS, TOLERABILITY AND SAFETY OF INTRAVENOUS IRON SUCROSE IN IRON DEFICIENCY ANAEMIA IN POSTNATAL WOMEN

DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT FOR

M.D DEGREE
BRANCH - II
OBSTETRICS & GYNAECOLOGY,
MADRAS MEDICAL COLLEGE,
CHENNAI - 3.

THE TAMIL NADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI - 1.

MARCH 2010

INDEX

KEY TO MASTER CHART

MOD - Mode of Delivery

1 – Labour Natural

2 – Labour Natural with Episiotomy

3 – Labour Natural with Lacerated Perineum

4 – Emergency LSCS

5 – Emergency repeat LSCS

6 – Emergency repeat LSCS with Sterilisation

OS - Obstetric Score

PS - Peripheral Smear

MH - Microcytic Hypochromic picture

TC - Total Count

SE - Side Effects

N - No Side Effects

H - Headache

T - Thrombophlebitis

C - Chills and Rigors

PROFORMA

STUDY OF EFFECTIVENESS, TOLERABILITY AND SAFETY OF INTRAVENOUS IRON SUCROSE IN IRON DEFICIENCY ANAEMIA IN POSTNATAL WOMEN.

Name : Age :

IP No : Address:

Occupation : Phone no:

Income :

Socioeconomic Class :

Obstetric score :

Para :

Live :

Abortions:

Presenting complaints:

H/o Easy fatiguability / giddiness

H/o Hook worm infestation

H/o Bleeding per vaginum

H/o Hematemesis / malena

H/o Anorexia / indigestion

H/o Multiple pregnancy

H/o Breathlessness

H/o Swelling of legs

H/o Puffiness of face

H/o Iron intolerance

Past H/o:

H/o Blood loss in between pregnancy

H/o DM, HT, Asthma, epilepsy, TB

Menstrual H/o:

Age at menarche :

Cycles : Regular Irregular

flow :

Marital H/o:

M /s :

Obstetric History :

Details about previous pregnancy:	Yes	No
H/o Antepartum Hemorrhage		
H/o Postpartum Hemorrhage		
H/o Blood Transfusion		

Present Pregnancy:

1. H/o Antepartum Hemorrhage
2. H/o Postpartum Hemorrhage

General Examination:

Features of Chronic anemia :	Yes	No
1. Pallor :		
2. Glossitis :		
3. Facial Puffiness :		
4. Koilonychia :		

VITALS

Temp:

PR : CVS :

BP : RS:

Investigations:

To confirm iron deficiency anaemia:

1. Hb :

2. Urine : Albumin

Sugar

Deposits

3. Blood : Sugar

Urea

Serum : Creatinine

5. Peripheral smear:

6. MCV

7. Hematocrit

8. Stool: Ova/Cyst

9. Serum iron:

10. TIBC:

11. Percent saturation:

Iron Requirement:

Dose of intravenous iron sucrose needed for therapy:

Parameters monitored during therapy:

Adverse effects	Yes	No
1. Anaphylactic reaction (Shivering, Hypotension)		

2. Nausea / Vomiting

3. Thrombophlebitis

4. Abdominal Pain

5. Diarrhoea

6. Chills / Rigors

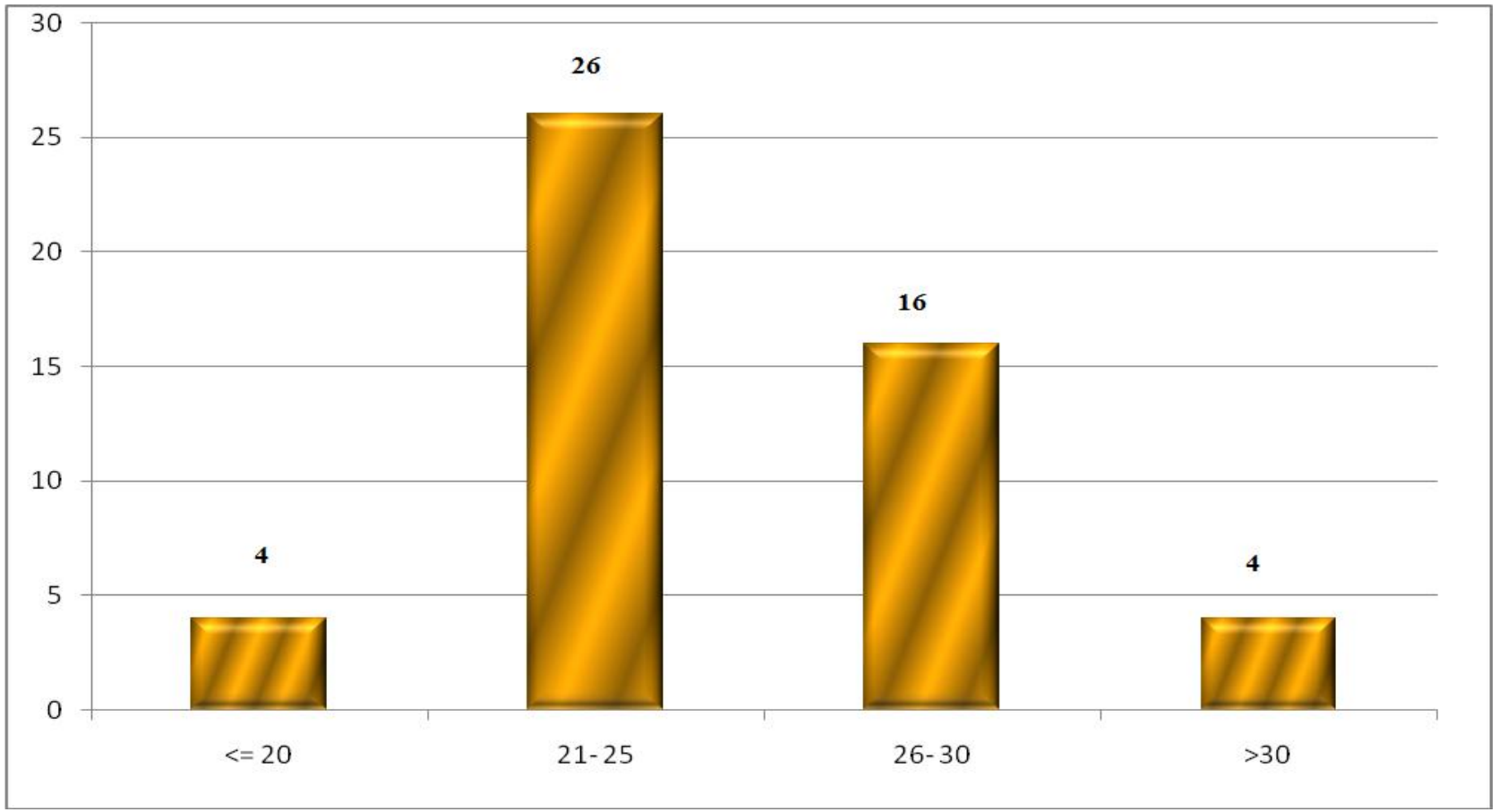
7. Joint pain

Post therapy Assessment:

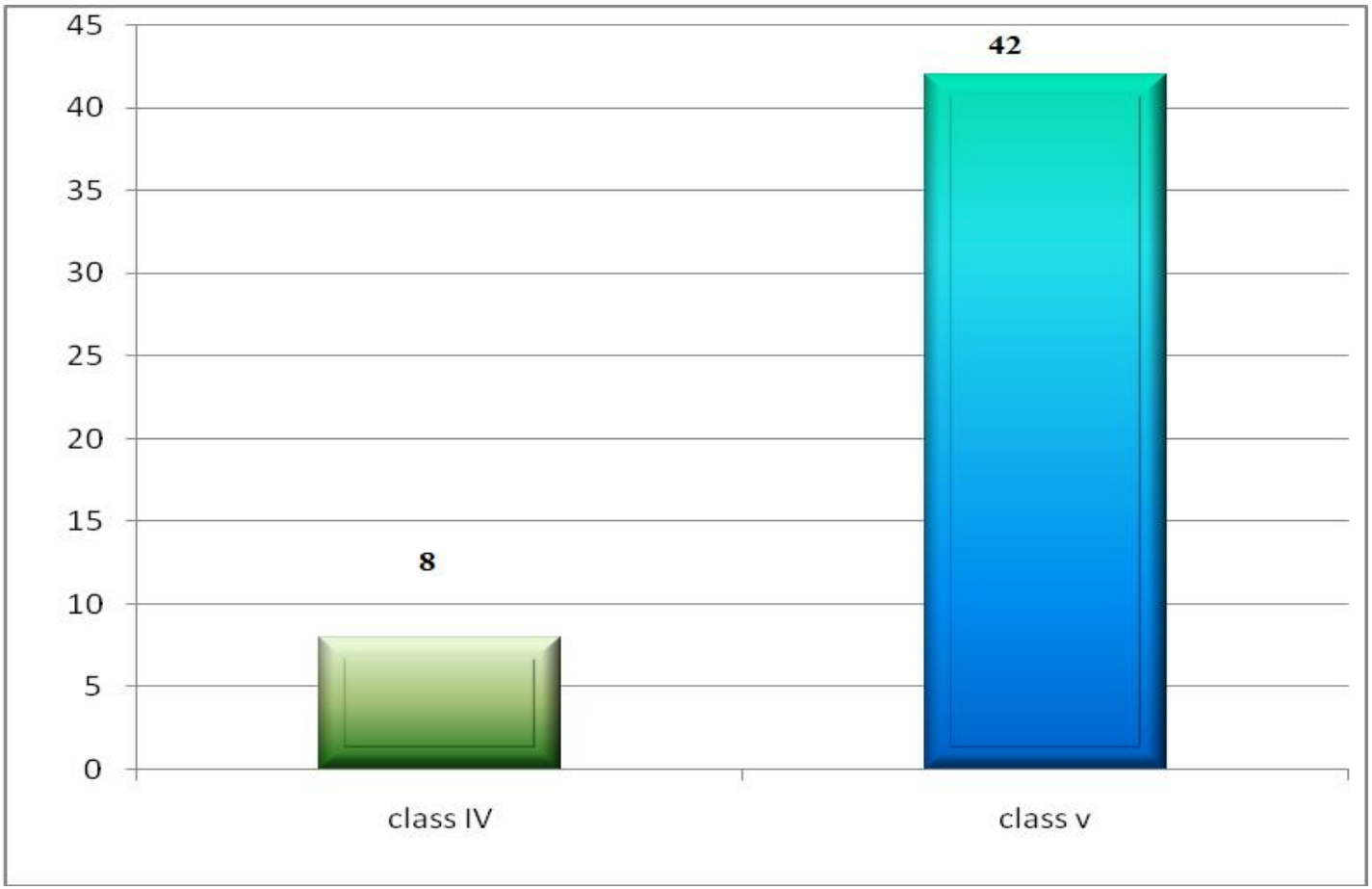
Parameters assessed 4 weeks post therapy

1. Hb
2. MCV
3. Hematocrit
4. Serum Iron
5. TIBC
6. Percent saturation

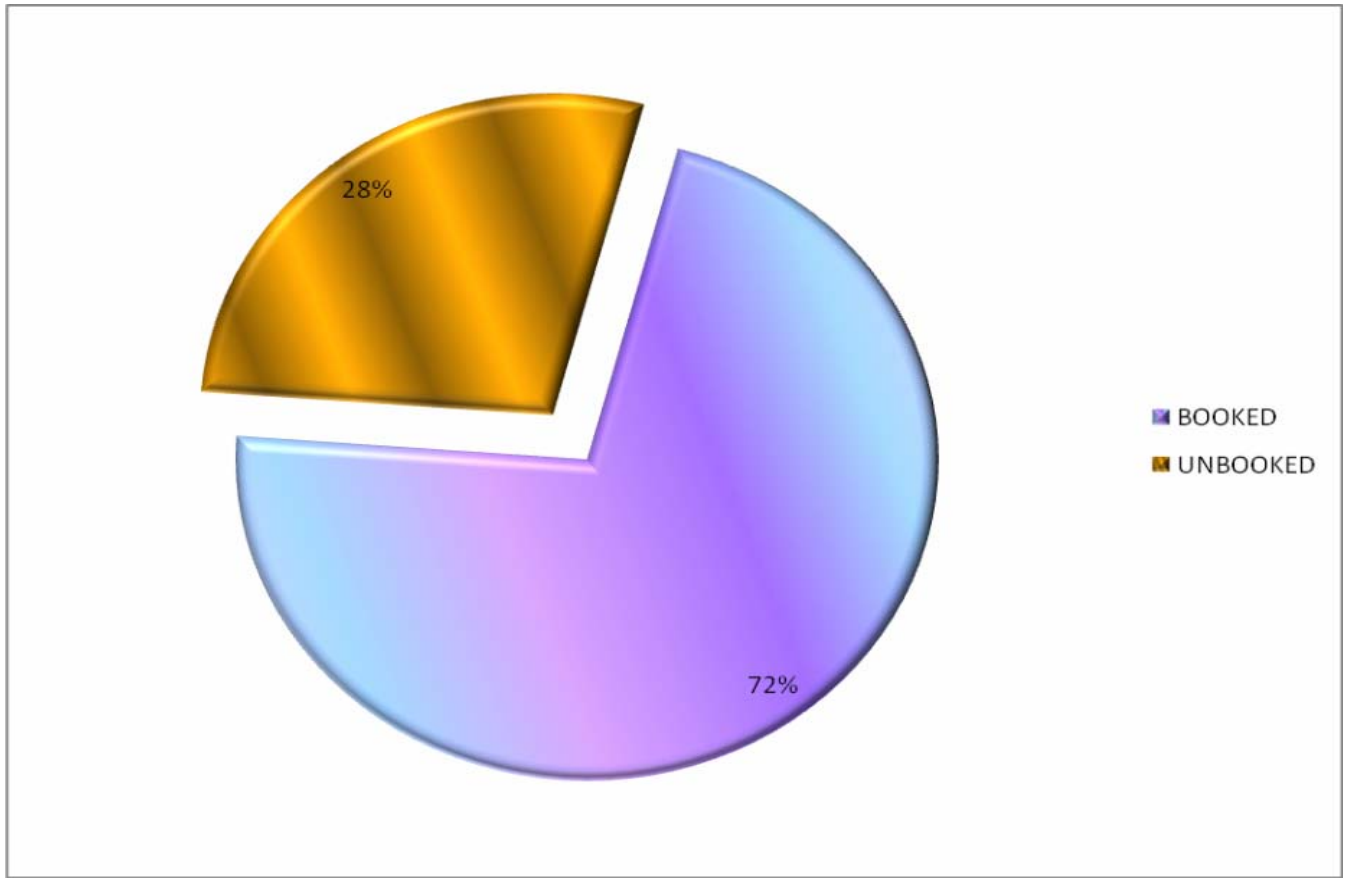
AGE DISTRIBUTION



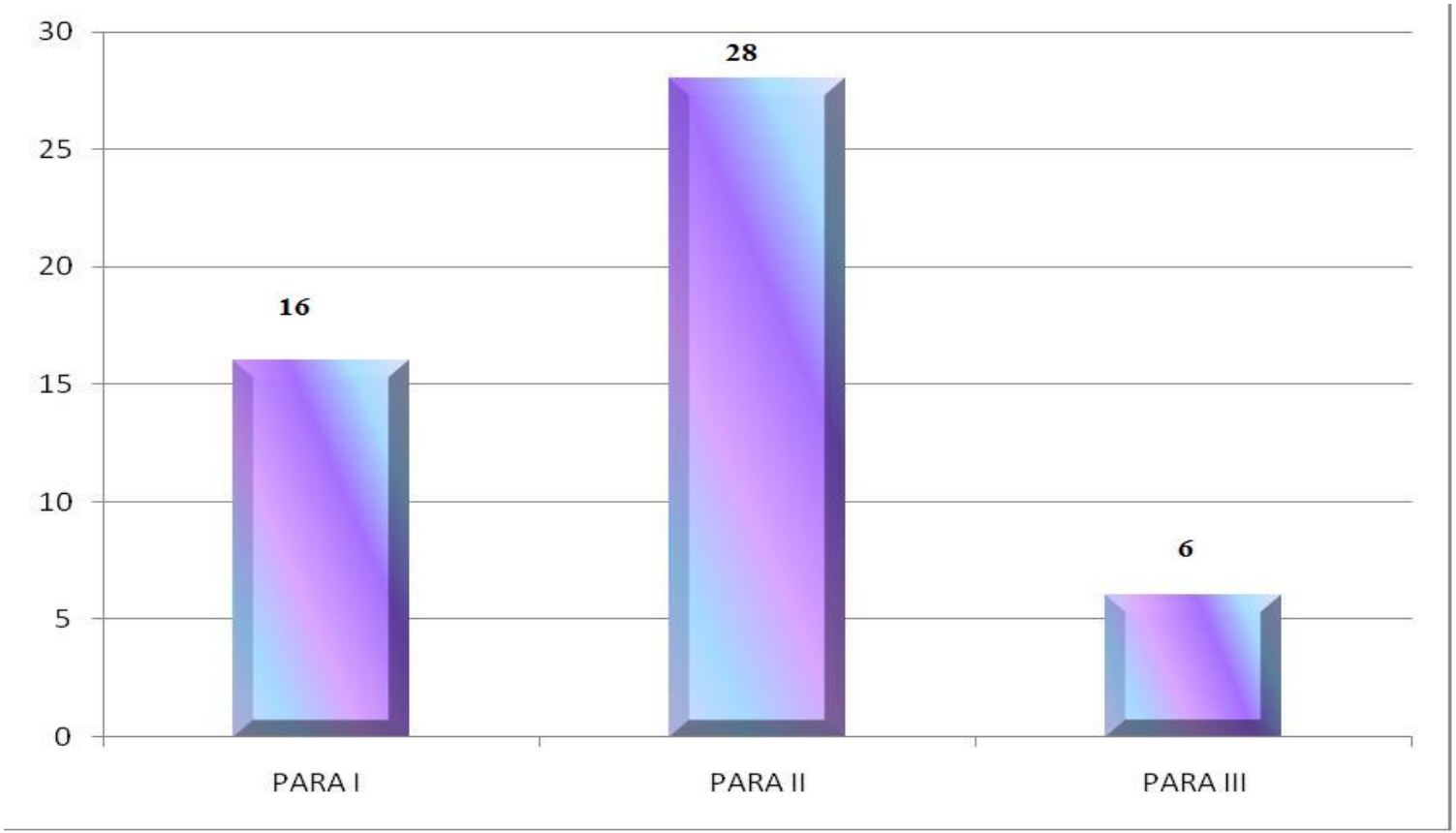
SOCIO ECONOMIC CLASS



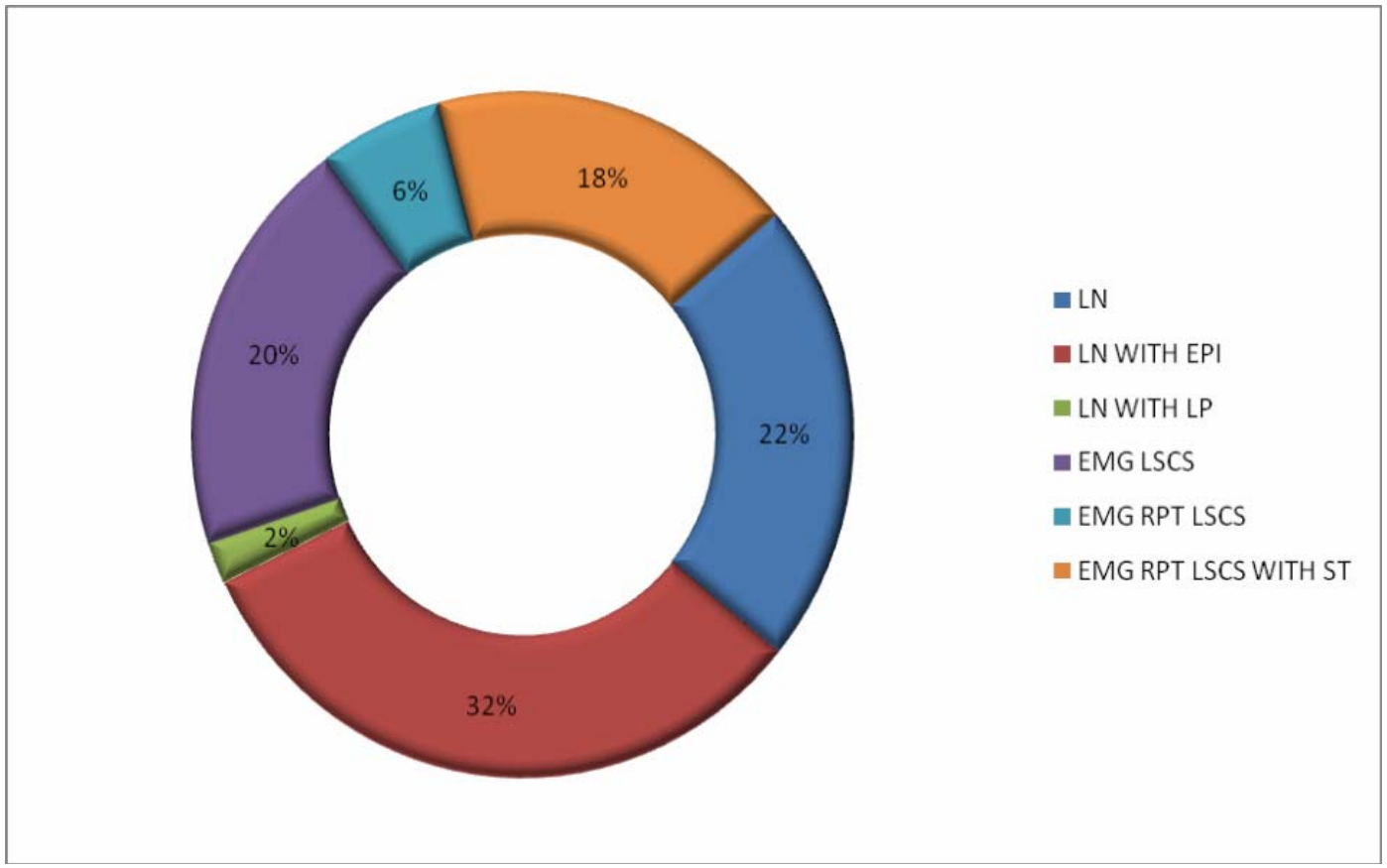
BOOKING STATUS



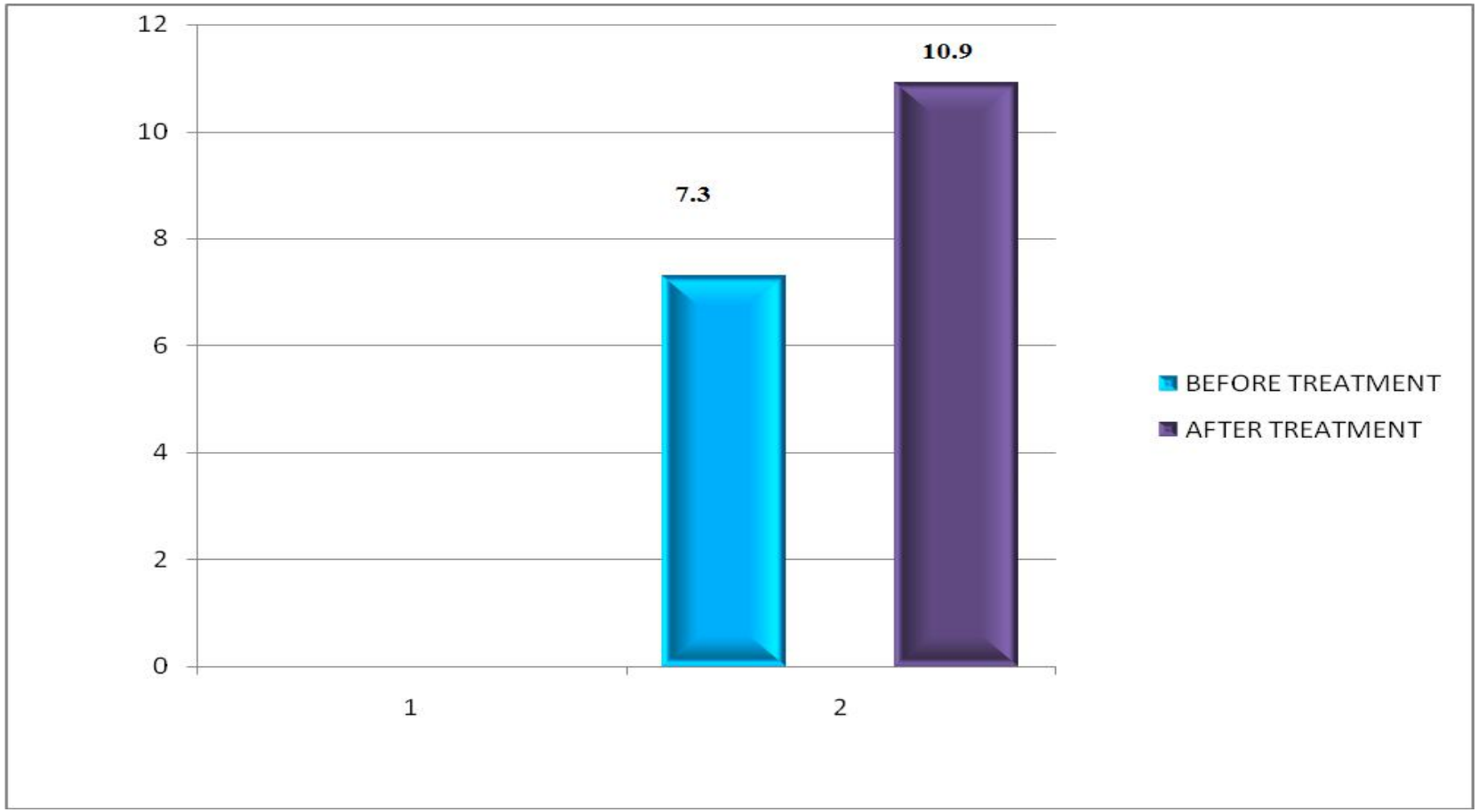
PARITY



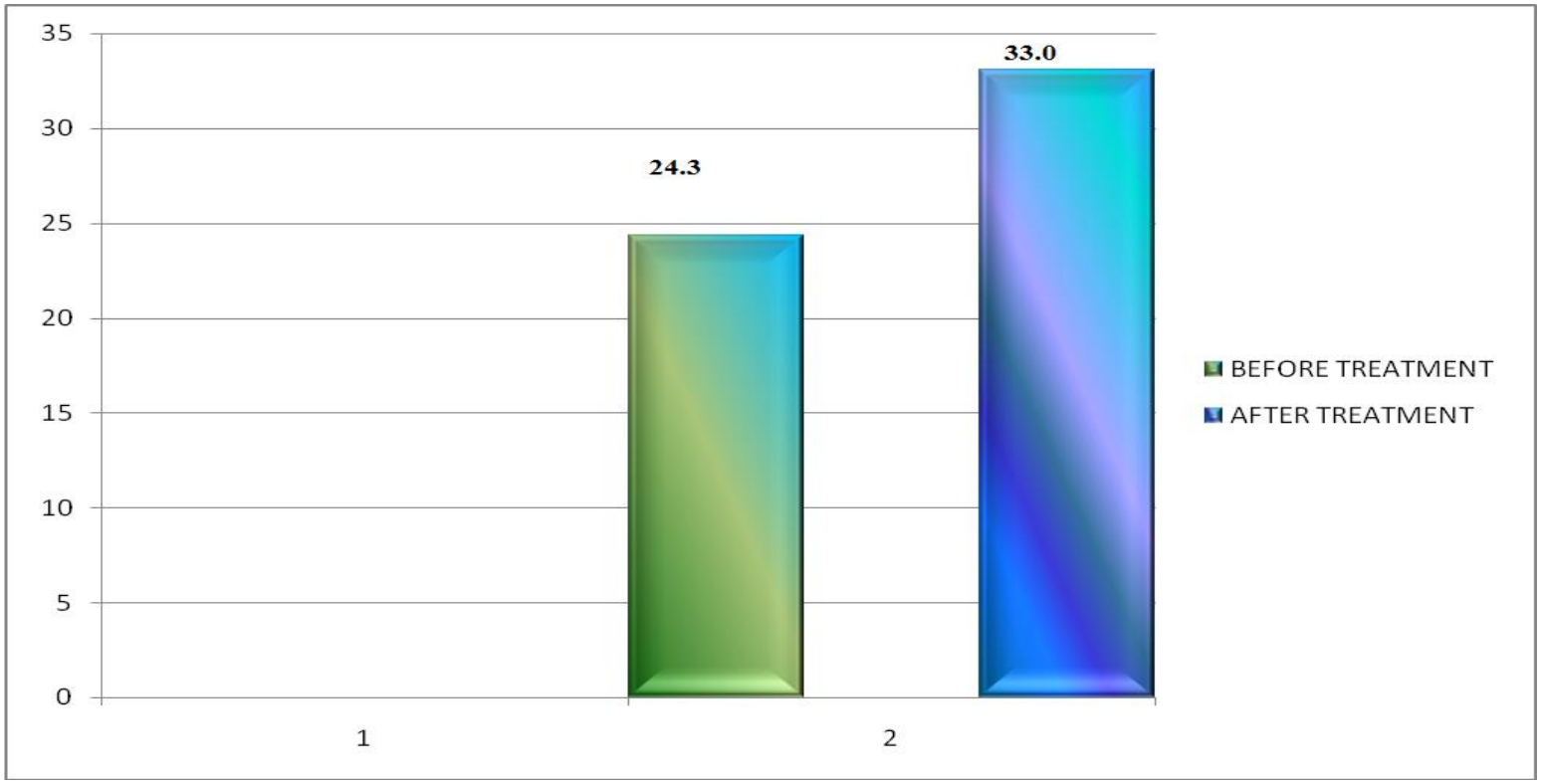
MODE OF DELIVERY



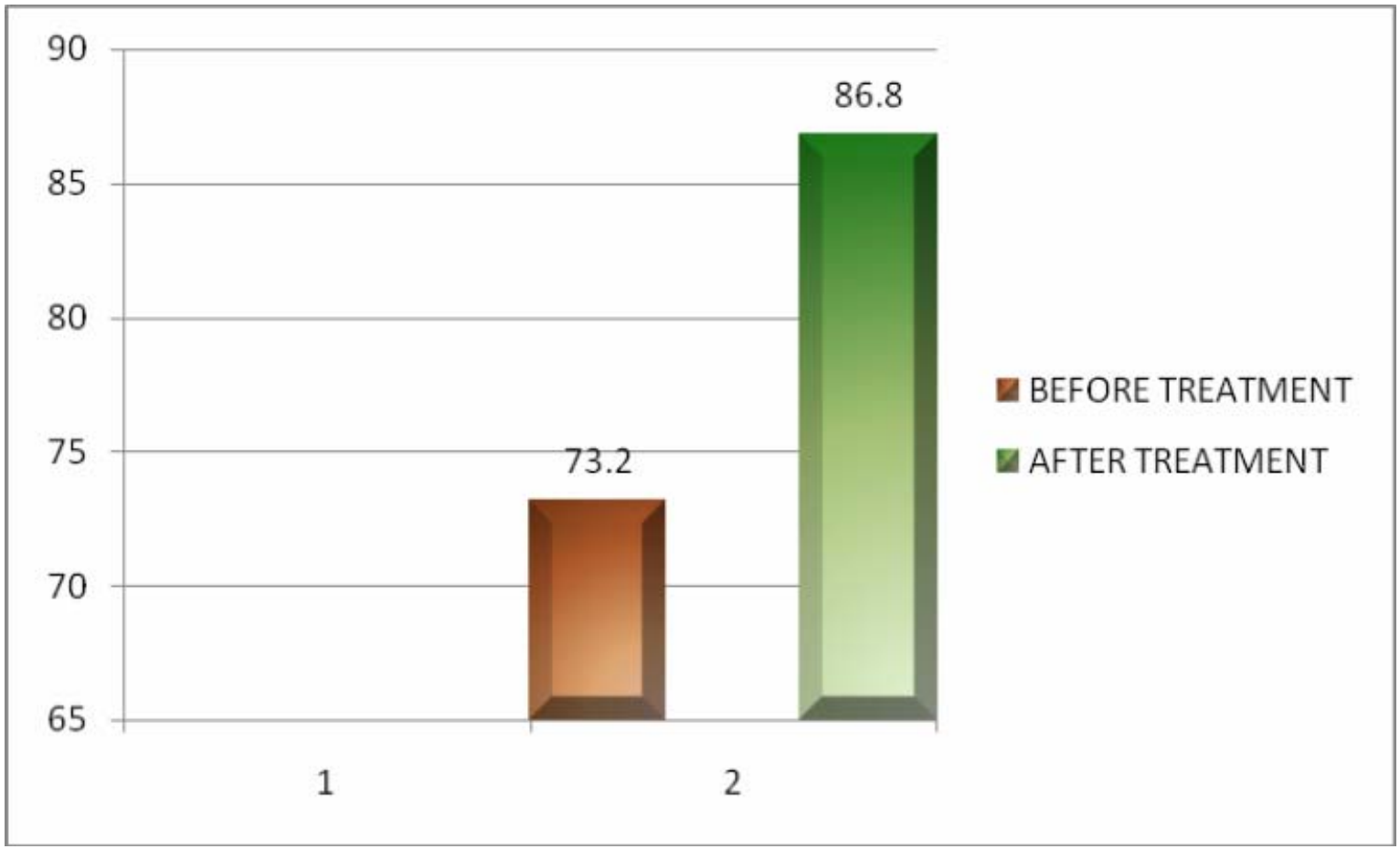
CHANGE IN HAEMOGLOBIN



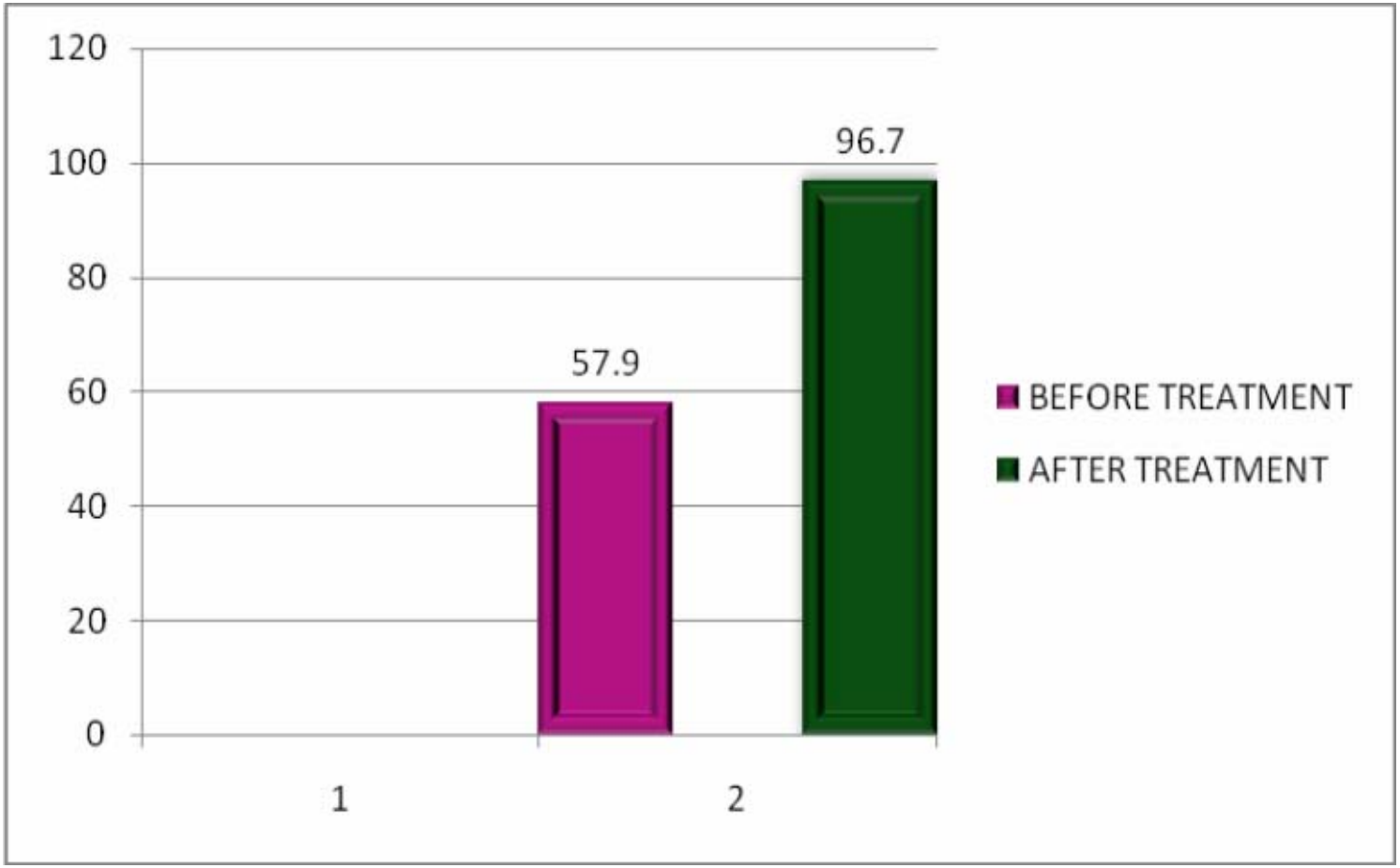
CHANGE IN HEMATOCRIT



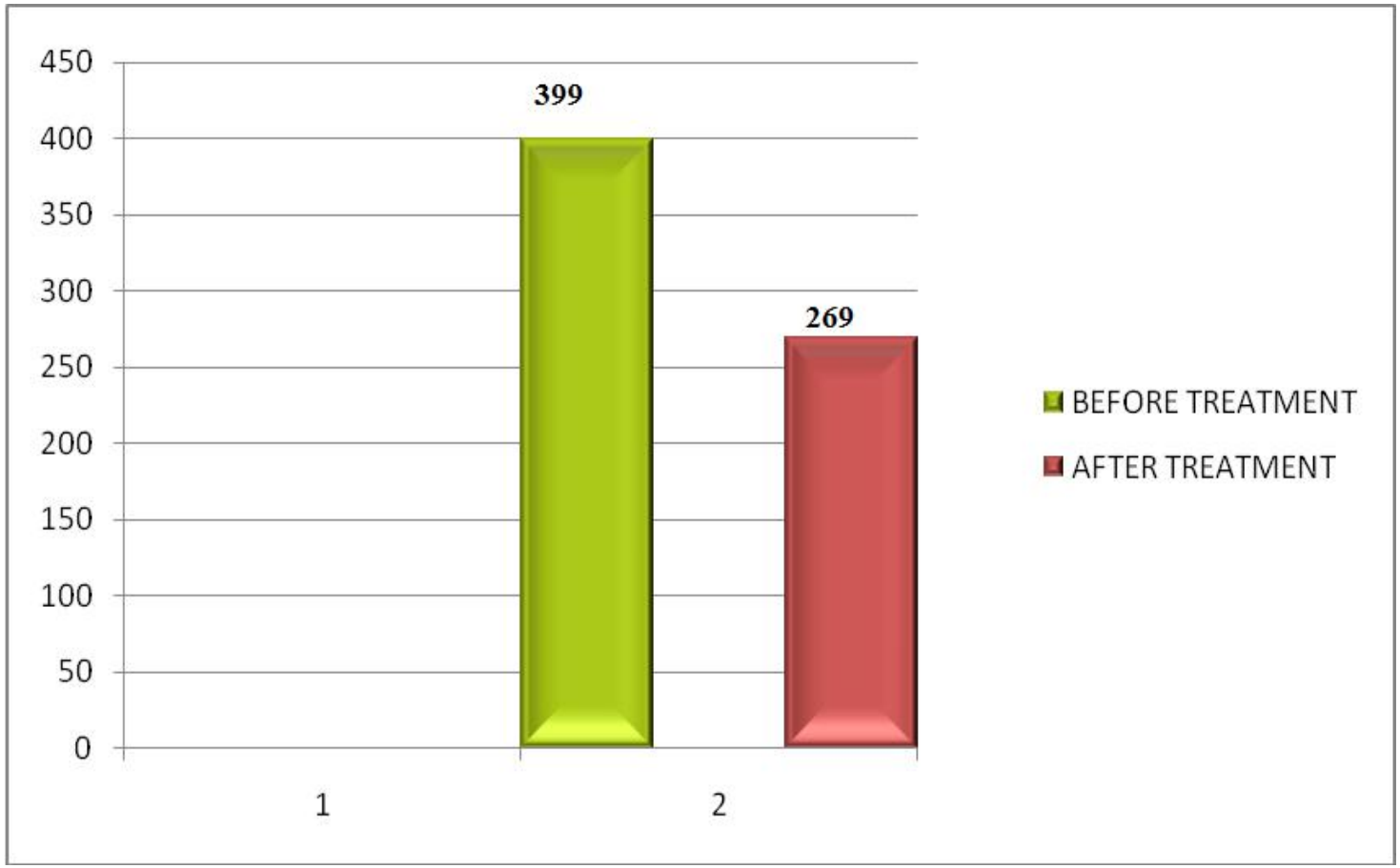
CHANGE IN MCV



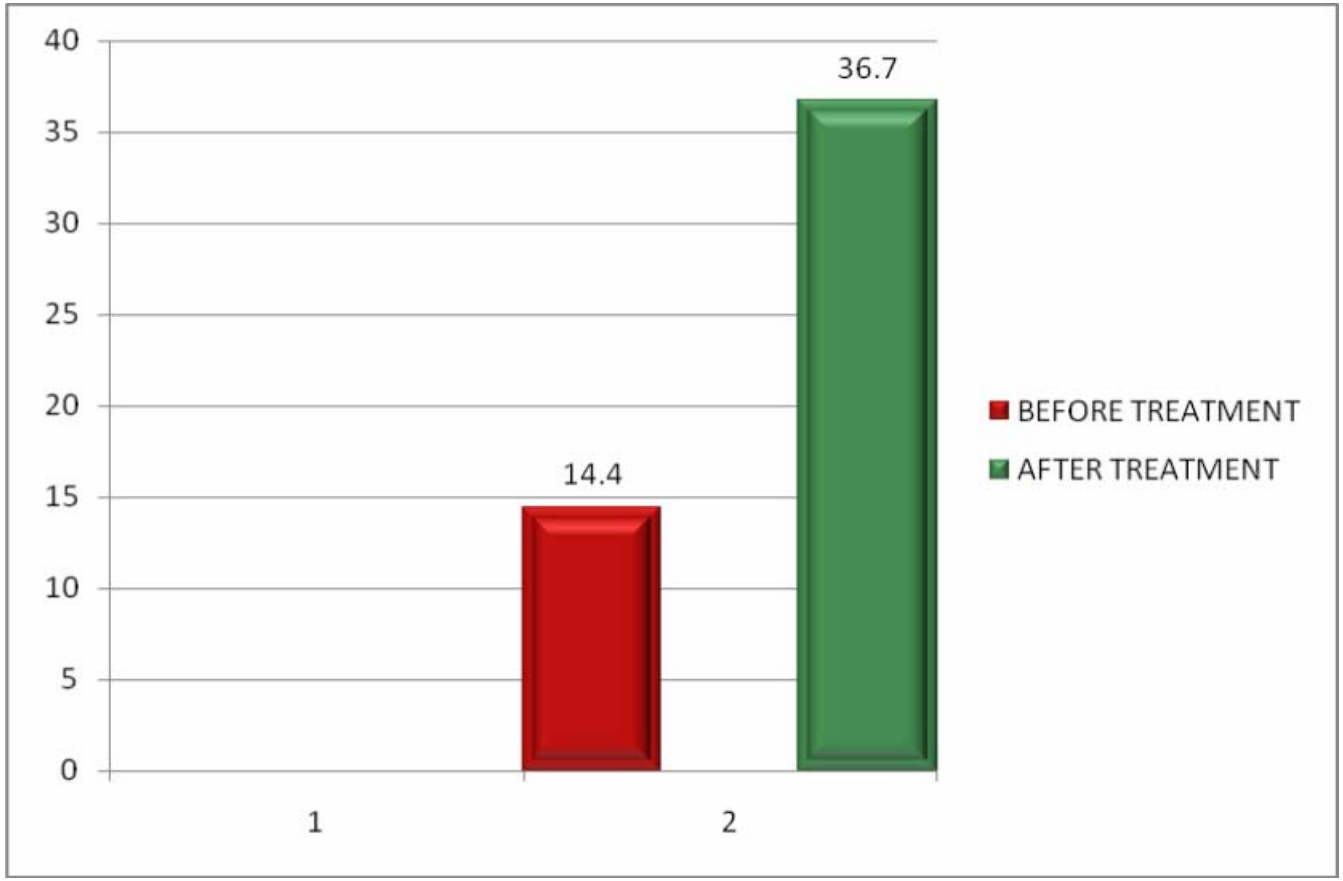
CHANGE IN SERUM IRON



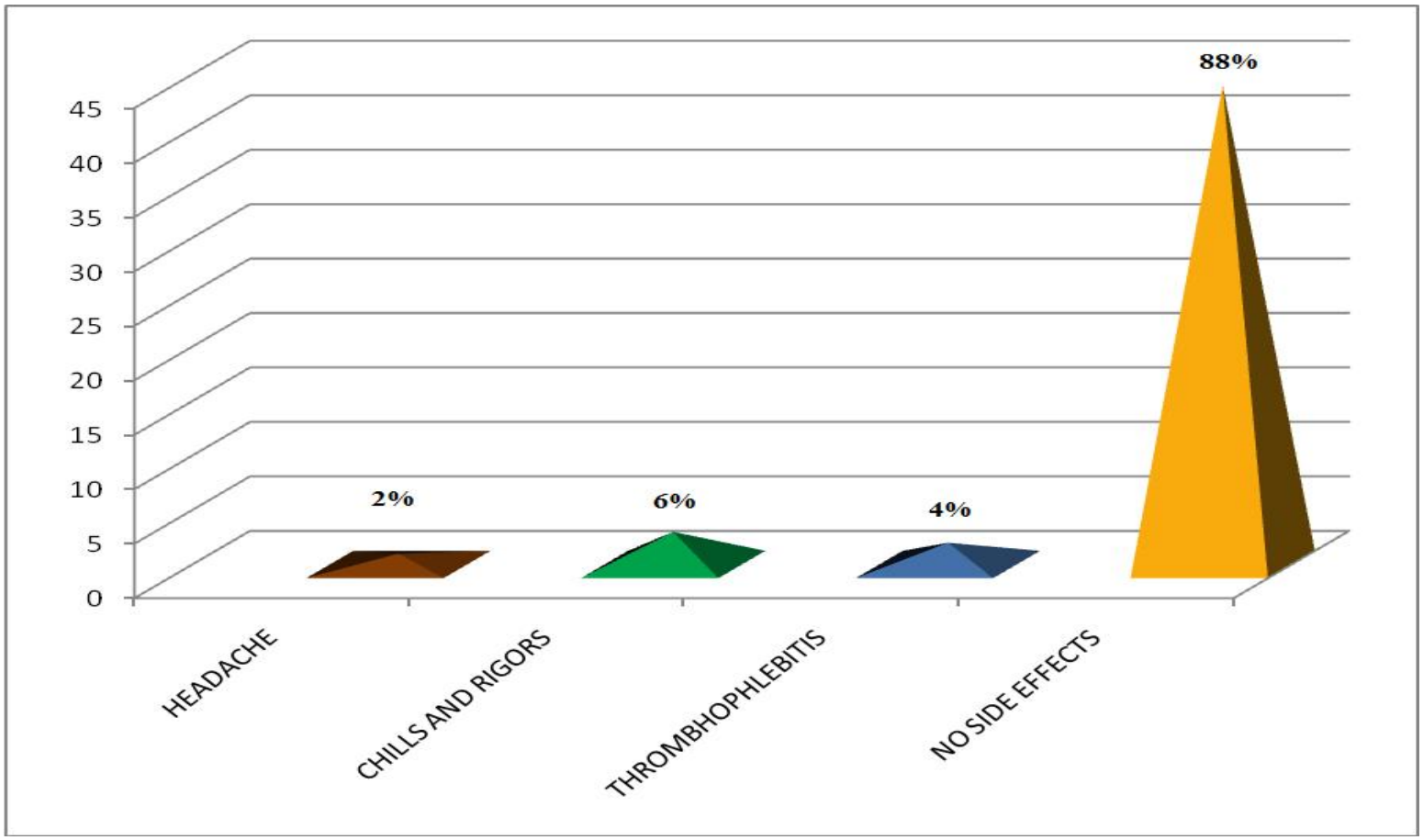
CHANGE IN TIBC



CHANGE IN PERCENT SATURATION



ADVERSE EFFECTS OF THE DRUG



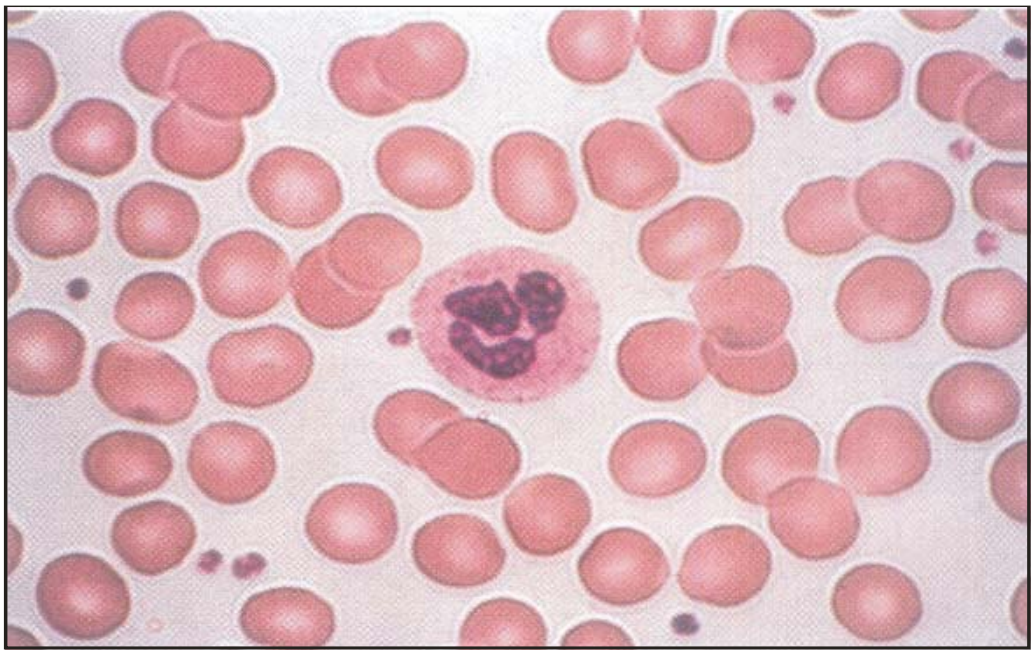
SERUM IRON AND TIBC REAGENT KIT

SEMI AUTO ANALYSER –ERBA CHEM PLUS V2

CELL COUNTER

IRON SUCROSE – HEMFER

NORMAL BLOOD PICTURE



PERIPHERAL SMEAR - IRON DEFICIENCY ANEMIA

Column1	Column2	Colu	Column	Colun	Column6	Colum	Colum	Colur	Colum	Colum	Colum	Colu	Columr	olumn1	olumn1	olumn1	olumn1	olumn1	Columr	Colu
S.No	Name	Age	IP.No.	MOD	OS	Hb%	PCV	MCV	S.IRON	TIBC	% sat	PS	TC	POST TRANSFUSION						
														Hb%	PCV	MCV	Sr.Ir	TIBC	% sat	SE
1	Velankanni	24	12608	2	P1L1	7.7	27	72.8	52	390	13	MH	7600	10.9	34.7	88	84	344	24.4	N
2	Saranya	22	12800	6	P2L2	6.5	20	63	50	410	12	MH	9300	9.7	30	86	82.4	345	23.9	N
3	Malar	23	12902	6	P2L2	6.9	24	65	49	395	12.4	MH	9000	9.7	33.3	87	92.5	236	39.1	N
4	Priya	24	13177	2	P1L1	7.3	21.8	76	58	412	14	MH	14700	11.0	34	88	94	240	39.1	N
5	Pavithra	32	13498	6	P3L2	8	26.5	80	62	370	16	MH	14000	12.5	36	92	92	213	43.1	N
6	Gracy	29	13202	4	P1L1	7.5	19.5	78	60	380	15	MH	15500	11.2	34.6	94	99	215	46	H
7	Padmavathy	21	13188	4	P1L1	8	26	78	56	420	13.3	MH	15100	12.5	37.7	94	94	243	38.6	N
8	Kalaiselvi	26	14131	1	P2L1	6.9	22	66	67	450	14.8	MH	17100	10.4	33	88	102	280	36.4	N
9	Jaya	31	12450	2	P2L2	8	27	72	59	412	14.3	MH	10000	11.2	34	90	102	215	47.4	N
10	Subhashini	23	12811	2	P2L2	7.3	27	74	64	401	15.9	MH	14000	10.3	33	82	96	304	31.5	N
11	Amuthavalli	26	12905	4	P1L1	8	27	77	62	410	15.1	MH	14100	10.4	33	83	100	245	40.8	T
12	Roja Rani	26	13645	2	P2L2	8	28	75	60	406	14.7	MH	12000	11.0	34	87	102	250	40.8	N
13	Uma	20	13128	2	P2L2	6.5	23	70	62	395	15.6	MH	15000	9	28	82	96	204	47	N
14	Anandhi	25	13381	2	P3L3	6.5	20	69	68.4	356.3	19	MH	14200	11.2	34	86	98	256	38.2	C
15	Vinodhini	21	13578	2	P1L1	7.4	29.8	78.8	56	376.2	14.8	MH	13100	12.5	37	90	102	260	39.2	N
16	Shakila	30	12853	4	P2L2	8	28	78	68.4	341	19	MH	12100	11.4	34.6	89	98	215	45.5	N
17	Indumathy	24	11750	2	P1L1	8	27	79	60	408	14.7	MH	12000	12	35	90	100	254	39.3	N
18	Abirami	26	13580	2	P2L2	7.4	27	80	52	400	13	MH	15100	10.6	34	86	98	300	32.6	C
19	Thilaga	28	13456	1	P2L2	7.1	26	76	60	390	15.3	MH	14000	11.5	34	89	104	300	34.6	N
20	Devika	22	13396	6	P1L1	8	28	78.7	54	402	13.4	MH	13400	11.5	33	88	114.3	310	36.8	N
21	Vasuki	24	14015	2	P1L1	6.6	20	63	56	370	15	MH	10000	9.4	28	83	98	300	32.6	N
22	Parameshwari	23	14030	4	P1L1	7.3	26	69	64	411	15.5	MH	13100	10.7	33	84	100	250	40	N
23	Thilagavathy	20	16834	1	P1L0	8	27.6	74	62	411	15	MH	11300	11.2	32.8	86	114	245	46.5	N
24	Alamelu	25	16894	1	P1L1	7.8	23.6	76	60	390	15.3	MH	11100	11.1	32	87	98	250	39.2	T
25	Kalavathy	25	16611	1	P2L2A2	6.4	23.8	65	52	410	12.6	MH	12100	10.1	31.6	85	88	300	29.33	N
26	Mariammal	20	16823	6	P1L1	7.4	26	69	62	380	16.3	MH	13100	10.8	31	88	92	280	32.8	N
27	Jayanthy	30	16862	4	P2L2	6.3	22	70	54	410	13.1	MH	14000	9.4	31	82	88	270	32.5	N
28	Sandhya	20	16928	5	P3L2	6.5	20	72	61	390	15.6	MH	12100	10.1	34.7	86	98	240	40.8	N
29	Amudha	22	16902	5	P2L2	7	21	78	60	415	14.4	MH	13200	11.4	35.2	90	108	215	50.2	N
30	Bhau nesha	23	17310	2	P2L2	6.1	20	60	51	400	12.7	MH	14100	9.1	28	85	84	300	28	N
31	Latha	24	18723	1	P2L2	7.4	26	75	52	490	10.6	MH	12100	11.2	33	84	88	305	28.8	N
32	Selvi	23	18757	1	P2L2	6.4	21	68	62	380	16.3	MH	11000	10.1	31	85	90	305	29.5	N

33	Madhumitha	24	18689	1	P2L1A1	7	22	69	62	390	15.8	MH	12000	11.1	33	88	110	288	38.1	N
34	Sandhya	23	19047	1	P2L2	8	27	77	60	400	15	MH	11000	12.7	35	89	99	290	34.1	N
35	Jayanthy	24	19105	1	P2L2	7.4	28	75	60	390	15.3	MH	12000	10.2	33	83	86	310	27.7	N
36	Madhavi	32	19309	6	p2L2	7	26	68	58	410	14.1	MH	13,300	11.3	35	86	103	280	36.7	N
37	Pusparani	24	18080	2	P2L2	8	28	80	60	410	14.6	MH	11100	11.1	33	85	92	300	30.6	C
38	Padmavathy	26	17640	6	P2L2	7.9	28	80	59	390	15.1	MH	13200	11.5	34	85	98	215	45.5	N
39	Vijayalakshmi	24	17277	2	P1L1	6.8	20.1	72	54	400	13.5	MH	10000	11.7	32.8	83	97	313	30.9	N
40	Komala	26	19047	4	P2L1	6.7	19.7	74	58	380	15.2	MH	17100	10.1	29.1	82	88	300	29.3	N
41	Prabha	28	19126	4	P2L2	6.1	20.9	63	46	420	10.9	MH	15400	9.7	30.1	87	92	280	32.8	N
42	Menaka	26	19134	4	P1L1	7.9	22.3	79	56	390	14.3	MH	13200	12.2	34.4	92	102	250	40.8	N
43	Ramya	26	19244	4	P2L3	6.1	18.9	62	52	390	13.3	MH	10100	9.7	30.1	87	92	280	32.8	N
44	Jayanthy	25	19256	5	P2L2	8	25.1	79	60	400	15	MH	11210	11.0	32.9	88	114	240	47.5	N
45	Akhilandeshwar	29	19360	6	P3L2	7.4	23.6	72	59	410	14.3	MH	13400	11.2	34	86	98	300	32.6	N
46	Meharunesha	28	19412	2	P3L3	7.2	23.3	77	60	400	15	MH	17500	11.4	34.1	87	88	290	30.3	N
47	Latha	27	19426	2	P1L1	8	25.1	78	54	400	13.5	MH	13000	11.2	33	84	88	305	28.8	N
48	Thangam	22	19434	1	P2L2A2	7.9	26	79	58	390	14.8	MH	12100	11.4	34.1	87	88	290	30.3	N
49	Malarvizhi	26	19500	6	P2L2	7.5	24	76	46	410	11.2	MH	12100	10.5	31.5	83	89.4	330	27.9	N
50	Janaki	25	19604	3	P3L3	8	28	78	60	390	15.3	MH	11000	12.2	36.3	94	94	243	38.6	N